

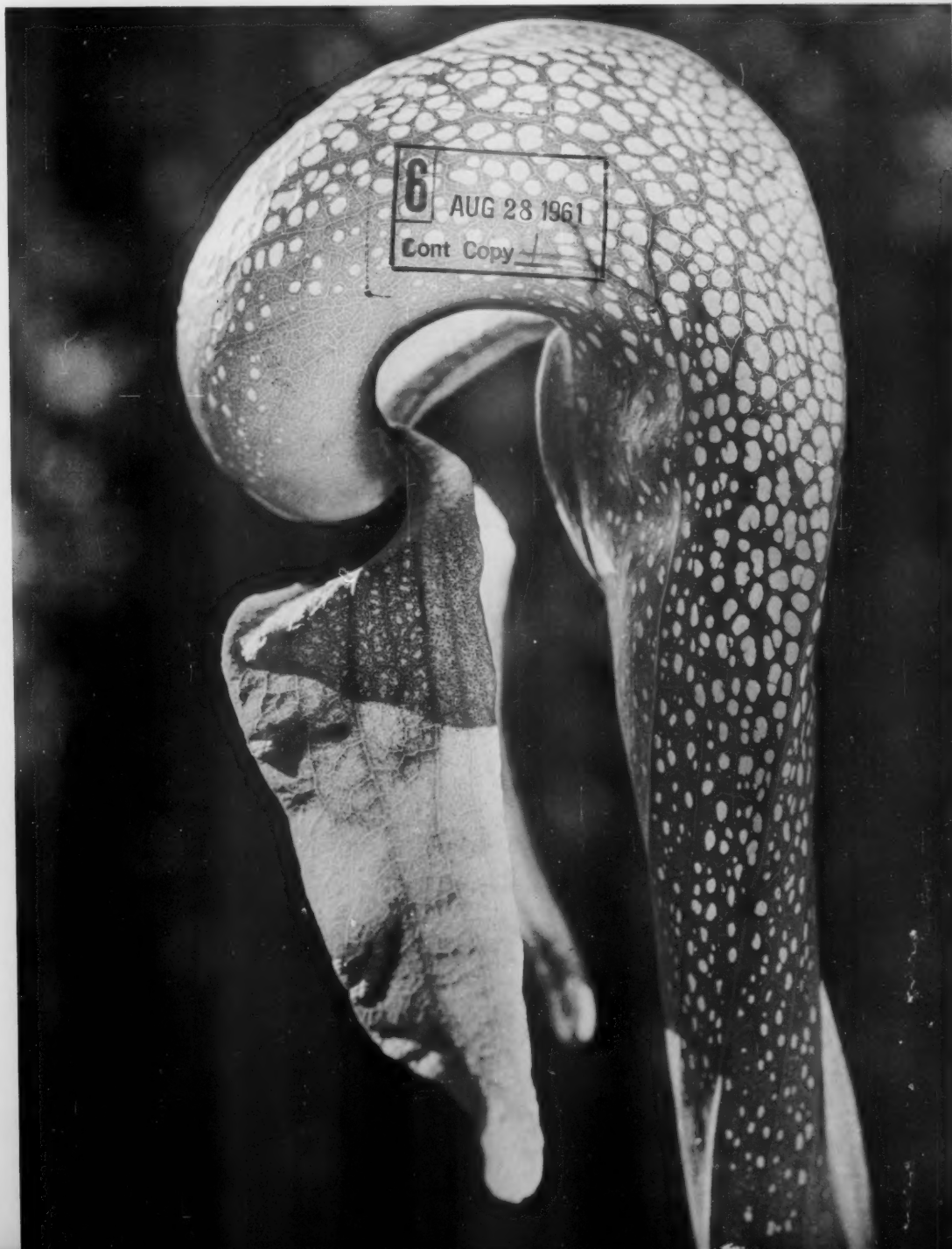
Sec. 15

# SCIENCE

25 August 1961

Vol. 134, No. 3478

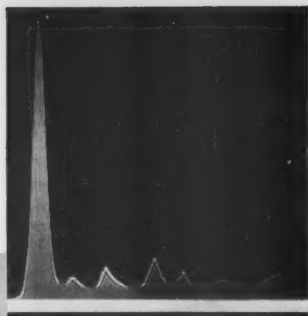
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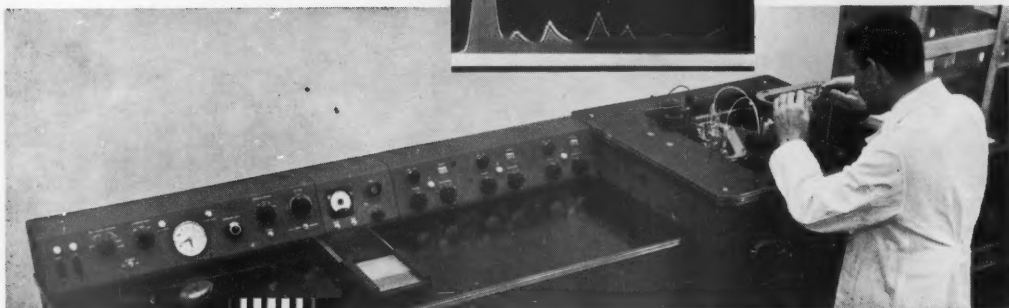
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*Electrophoresis of human plasma diluted 1:6; ascending boundaries. Inclined knife-edge schlieren.*



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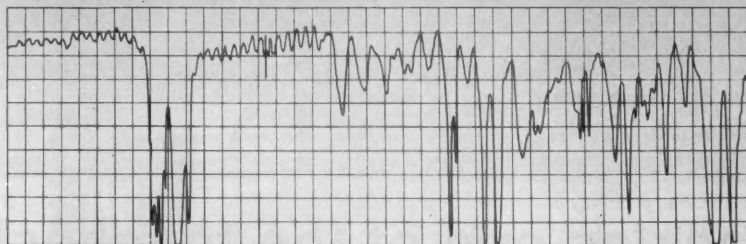
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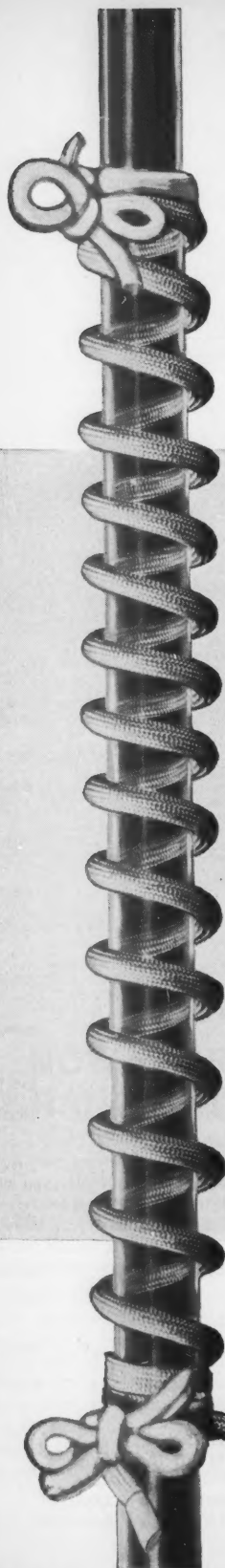
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<b>Cover</b>	Leaf of the unusual <i>Darlingtonia californica</i> , or western pitcher plant, a native of northern California and adjacent Oregon. Like other carnivorous plants of this group, the tubular base constitutes a liquid-filled trap; at the top the leaf is strikingly translucent. The general resemblance to a snake's head has suggested another common name—cobra plant. [W. H. Hodge, Kennett Square, Pa.]	



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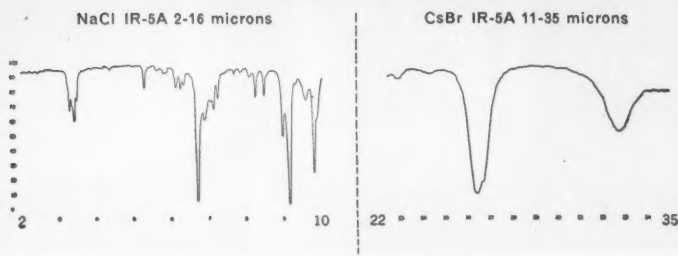


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## Letters

### Tumor Development

With reference to the report by H. K. Mitchell which appeared in *Science* [133, 876 (1961)], we should like to make the following comment.

That our preliminary investigations of tumor-inducing factor (TIF) have proved successful is shown by the fact that they have stimulated further related investigations in the field of mammalian carcinogenesis. These initially crude methods have led to the development of different bioassay techniques and refined purification procedures which are now being successfully applied to a broad study of tumor development in our laboratories as well as elsewhere. In addition, it has led to the study of tumor breakdown in mammalian hosts.

It would serve no useful purpose to engage in a vituperative exchange over techniques that have already served to stimulate a new approach to the cancer problem. We regret that Mitchell did not choose a more pleasant method of approaching the problem, but we will comply with his request and make no further reference to his participation in the early, historical aspects of this research.

LAWRENCE BURTON  
FRANK FRIEDMAN

*Hodgkins Disease Research  
Laboratories, St. Vincent's Hospital,  
New York, New York*

### Satellite Communication

I think that it is unfortunate that the primary issues of satellite communication were so lost and beclouded in the news note "Space communications" [*Science* 133, 1812 (1961)].

In principle, communication satellites could afford valuable international communication, first by linking the highly developed but inadequately interconnected common-carrier communication networks of Europe and North America, and later by improving communication

with other parts of the world. Such a peaceful use of space would certainly be to our credit, and the more so the sooner it was attained.

I have noted in "Hazards of satellite communication" [*Bull. Atomic Scientists* (May 1961)] that this will not be easy technically, and that nontechnical obstacles could delay it indefinitely.

Thus, I think it is very misleading to say, with John Finney, that the direct issue is, "who shall sow and who shall reap the first big financial dividends of the space age." Much more direct issues are: Can satellite communication useful to the people of the world be brought into being quickly, and if so, how can this be done? When these questions are answered, we may then, if we wish, seek to meet reasonable standards of regulation and ownership. But, to give primarily political questions precedence over the realities of technology and the realities of international communication could delay satellite communication indefinitely.

One reality of international communication is that you can pick up your telephone and call a person in any one of over 160 different political areas in all parts of the world. Through the International Telecommunications Union, which is almost a hundred years old and which is now a part of the United Nations, and through its organs, international agreements on the use of frequencies and on standards and operating procedures have been worked out. Agreements for communication and agreements involving the shared ownership of international cables have been brought into effect. In the face of this existing international situation, it seems chauvinistic and arrogant to the point of madness to suggest that the United States Government or any purely American company or group of companies *could*, by itself, own an international satellite communication system.

The research and development necessary to make a satellite communication system possible is an entirely different

matter. We cannot afford to have this wait on the formation of a new company. NASA's Project Relay is a natural step. So is the Bell Laboratories' work, which A.T.&T. is financing. Why should obstacles be put in the way of any research and development at this time?

Like ships, boosters are now among us, a resource of man. Must only the government take advantage of this resource? The electronic and communication arts, which provided the transistor and the solar cell, are largely the products of work done by private enterprise without government support. Should the government be forbidden to use transistors and solar cells in space? Who is giving away what, and to whom?

The question, "Does private industry have the capital, and so on" is completely unrealistic. A proper question is, Do the common-carrier communication systems of the world have the capital? (Most of these aren't private-enterprise systems.) The answer is yes. This is demonstrated by the continued growth in international submarine telephone cables, an art comparable to satellite communication in difficulty and cost.

Must the very first satellite communication system connect us with all the underdeveloped countries, where internal communication itself is poor? How long should we wait to make sure that these will be included? Until the Russians have satellite communication first?

The chorus of "You shan't have satellite communication unless" is already too loud. I hate to see *Science* embroiled in this windy, empty, but terribly dangerous debate.

J. R. PIERCE

275 McMane Avenue,  
Berkeley Heights, New Jersey

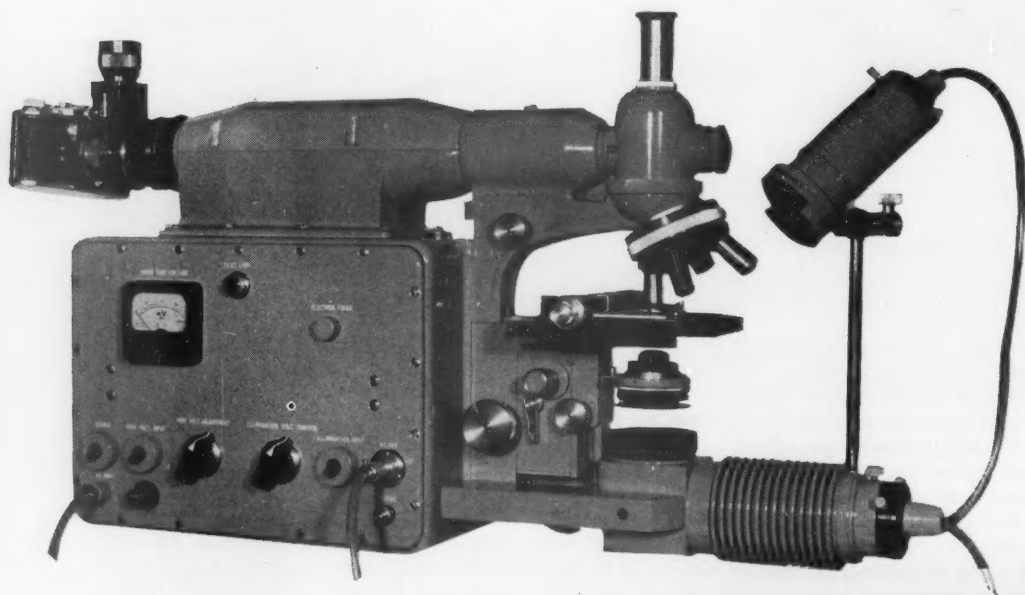
### Communication Channels

I would like to comment briefly on certain statements made by H. H. Goldstine in the article on information theory which appeared in a recent issue of *Science* [133, 1395 (1961)].

After discussing the concept of channel capacity for discrete noiseless channels, defined by Shannon in his classical paper [C. E. Shannon, *Bell System Tech. J.* 27, 379, 623 (1948)], as the limit, as  $T \rightarrow \infty$ , of  $[\log_2 N(T)]/T$ , where  $N(T)$  is the number of distinct messages of duration  $T$ , Goldstine proceeds to discuss the noisy communication channel and makes the curious statement that the coding theorem for such channels, "...

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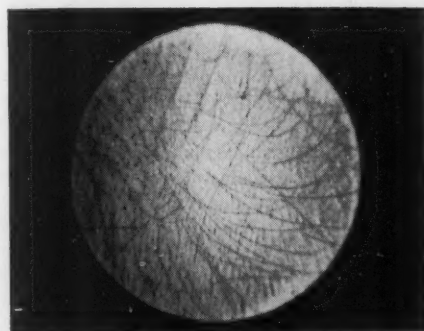
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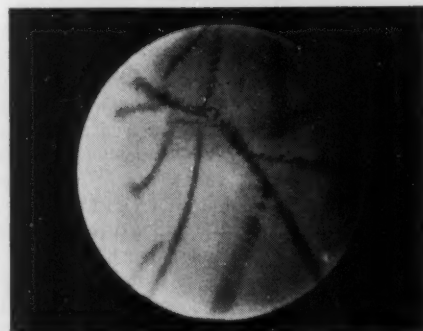
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roughly speaking, guarantees that the channel capacity as just defined is precisely the maximum rate at which it is possible to receive information with arbitrarily high reliability."

Are we to conclude, then, that by the use of an appropriate encoding procedure the information rate through a noisy channel may be brought arbitrarily close to the channel capacity of the corresponding noiseless channel? Apparently so, for the article continues, "A priori, one might imagine that as the noise in a channel increases, the rate at which one can transmit information . . . down the channel would necessarily decrease to zero." The clear implication that such a decrease does not occur leaves us with the impression that there have been revolutionary (and unpublished) developments in communication theory such that the degradation of communication channels by noise now arises only because of the absence of suitable encoders and decoders. Of course, Shannon's coding theorem for a noisy channel is actually a proof that it is possible, by suitable coding to communicate information even in the presence of noise at a definite rate and with an arbitrarily small frequency of errors, although this rate is naturally lower than that for the corresponding noise-free channel. The theorem is based on a definition of channel capacity

$$\max [H(x) - H_e(x)]$$

where  $H(x)$  is the source entropy,  $H_e(x)$  is the equivocation, and the maximization is carried out over all possible information sources used as input to the channel. It is in the definition of equivocation that the channel noise enters the theory and reduces the channel capacity from the value for the corresponding noiseless channel.

ALAN B. LEES

Systems Laboratories Division,  
Electronic Speciality Company,  
Los Angeles, California

Lees has been good as to call my attention to an ambiguously worded sentence in my article. This sentence which appears on page 2, column 1, is quite unambiguous if it is changed to read as follows: "This theorem, roughly speaking, guarantees the existence of a non-zero rate at which it is possible to receive information with arbitrarily high reliability."

H. H. GOLDSTINE

Thomas J. Watson Research Center,  
International Business Machines Corp.,  
Yorktown Heights, New York

25 AUGUST 1961

## Identification of Aldehyde in Mars Vegetation Regions

In an article in *Science* (1), W. M. Sinton reported three infrared bands, at 3.67, 3.56, and 3.43  $\mu$ , respectively, which he found in the vegetation regions of Mars but not in the desert regions. These bands he identified as being due to the presence of carbon-hydrogen linkages, and therefore to organic material in these areas. He also mentioned that terrestrial plants have bands in the region 3.56 to 3.43  $\mu$  but that the strong band at 3.67  $\mu$  is not found in terrestrial plants.

While there are many organic materials with bands in the region 3.56 to 3.30  $\mu$ , there are very few materials of any type with a prominent band at 3.67  $\mu$ , so a possibility of specific identification presented itself.

Most organic aldehydes (but not formaldehyde) have bands at 3.65 to 3.70  $\mu$  and 3.53 to 3.56  $\mu$ , due to the aldehyde carbon-hydrogen linkage, and they are among the few materials with a strong band near 3.67  $\mu$ . As is indicated in Fig. 1, the band at 3.67  $\mu$  is probably due to the aldehyde group, which also contributes to the band at 3.56  $\mu$ . The band at 3.43  $\mu$  is probably due, as Sinton states, to the carbon-hydrogen linkages in carbohydrates and protein organic matter in plants which resembled terrestrial plants, although an exact identification is difficult, due to the extremely large number of materials with carbon-hydrogen bands which absorb in this region (2). The most likely aldehyde is acetaldehyde, since most other aliphatic aldehydes have more nonaldehydic carbon-

hydrogen than is indicated in Sinton's data, but some other aldehyde is a possibility. The presence of the terrestrially reactive aldehyde is perhaps a reflection of the near absence of oxygen on Mars and the consequent lack of oxidation.

If I may be permitted to speculate a bit, acetaldehyde may be an end product of certain anaerobic metabolic processes. A familiar one is the metabolic fermentation of carbohydrates to acetaldehyde and then to alcohol (3). This process yields much less energy for the organism than conventional oxidation (carbohydrate + oxygen  $\rightarrow$  CO<sub>2</sub> + H<sub>2</sub>O + energy), but certain organisms on earth use fermentation as their source of energy when oxygen is not available, and perhaps this happens on Mars.

N. B. COLTHUP

Stamford Research Laboratories,  
American Cyanamid Company,  
Stamford, Connecticut

### References

1. W. M. Sinton, *Science* **130**, 1234 (1959).
2. L. J. Bellamy, *The Infrared Spectra of Complex Molecules* (Methuen, London).
3. J. H. Rush, *The Dawn of Life* (Hanover House, Garden City, N.Y.).

I am pleased to see Colthup's interpretation of the spectra of Mars.

It has been brought to my attention that in my article the wavelengths one would conclude from Fig. 2 (namely, 3.45, 3.58, and 3.69  $\mu$ ) do not agree with those that are stated. The precise wavelengths are difficult to determine. The instrumental width was 0.06  $\mu$  in the best spectra. For calibration I relied largely on atmospheric absorptions. A polystyrene film and a mercury arc were used in addition, but there were some erratic shifts in calibration, and it was felt that more reliable calibration was obtained by measuring atmospheric bands in the same spectra that were used for measuring the bands.

From the spectra obtained in 1958, the wavelengths from Fig. 2 of my article seem more reliable than the ones stated in my article. However, more spectra, which were of inferior quality, were obtained in 1960. From these new spectra I obtained values which are in agreement with those stated in the article. My conclusion is that the most reliable wavelengths are 3.45, 3.58, and 3.69  $\mu$ , with a possible error of 0.02  $\mu$ . These revised wavelengths are still in agreement with Colthup's interpretation.

WILLIAM M. SINTON  
Lowell Observatory, Flagstaff, Arizona

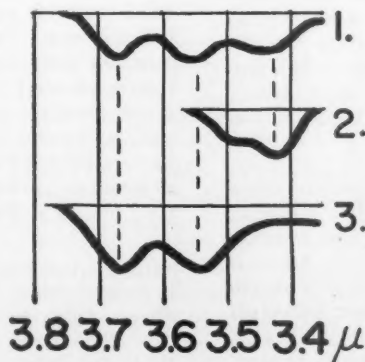
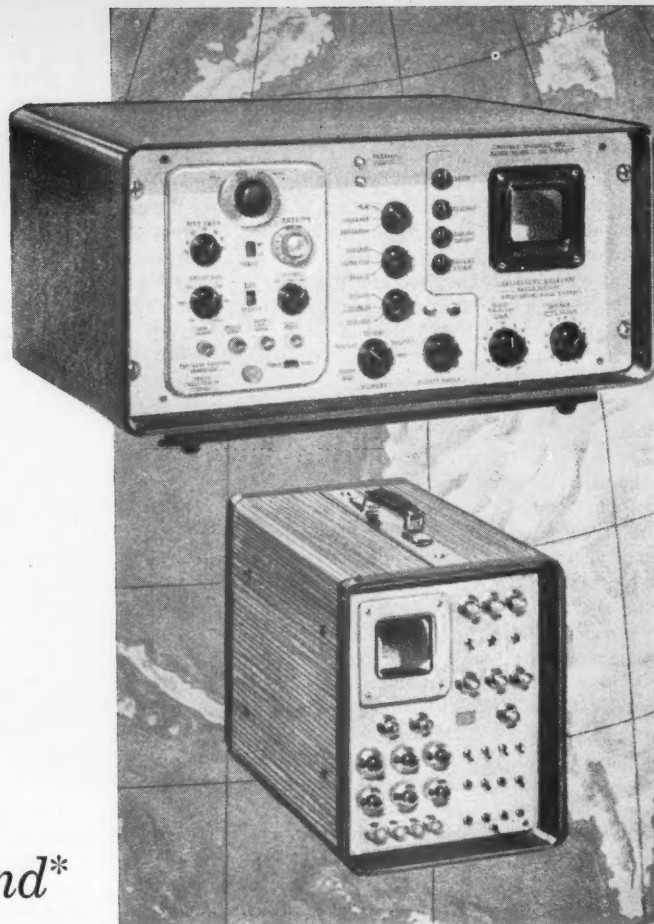


Fig. 1. (1) Infrared bands found in the Martian vegetation regions but not in the Martian deserts [adapted from *Science* **130**, 1234 (1959)]; (2) infrared bands in flour (terrestrial organic material); (3) infrared bands in acetaldehyde.

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## A Machineless Teaching Machine

Instructions: Cover the items below with a piece of paper, lowering the paper item by item as you read. For each item fill in the blank spaces. The words in parentheses that preface the *next* item give the correct response. Use reasonable judgment in deciding whether your response is synonymous with the printed response. Now, read the items.

To determine whether a student has understood a point, a teacher may \_\_\_\_\_ him a question.

(ask) If the student gives an incorrect answer, the teacher may tell him the \_\_\_\_\_ answer.

(correct) Sometimes a teacher will \_\_\_\_\_ a student a question and then, if necessary, tell him the \_\_\_\_\_ answer.

(ask, correct) Confirmation of success is also a part of pedagogy. If the student gives the correct answer, then he receives \_\_\_\_\_ of success.

(confirmation) If the student answers correctly, his success is \_\_\_\_\_; if he answers incorrectly, the teacher tells him the \_\_\_\_\_ answer.

(confirmed, correct) A fast learner likes to advance rapidly, while a slower learner is happier at a slower rate, each student advancing best at his own \_\_\_\_\_.

(rate) It would require an individual tutor for each student to insure that each student advanced exactly at his \_\_\_\_\_ rate.

(own) The teacher of a classroom is not able to insure that each student advances exactly at his \_\_\_\_\_.

(own rate) A teaching machine presents a sequence of statements, one at a time, to the student. The student writes his responses on a strip of paper accessible through an opening in the machine. Each statement, in effect, \_\_\_\_\_ the student a question.

(asks) The student then operates the machine to make his written response inaccessible, but visible through a window, and to reveal the correct response for comparison. If the student is correct, his success is \_\_\_\_\_; if he is incorrect he is told the \_\_\_\_\_ answer.

(confirmed, correct) A teaching machine is like a teacher in that the student is \_\_\_\_\_ questions, his successes are \_\_\_\_\_, and his mistakes are \_\_\_\_\_.

(asked, confirmed, corrected) A teaching machine has the advantage of an individual tutor in that each student proceeds at exactly his \_\_\_\_\_.

(own rate) An ordinary textbook also allows each student to proceed at his \_\_\_\_\_, insofar as he is able to proceed by himself.

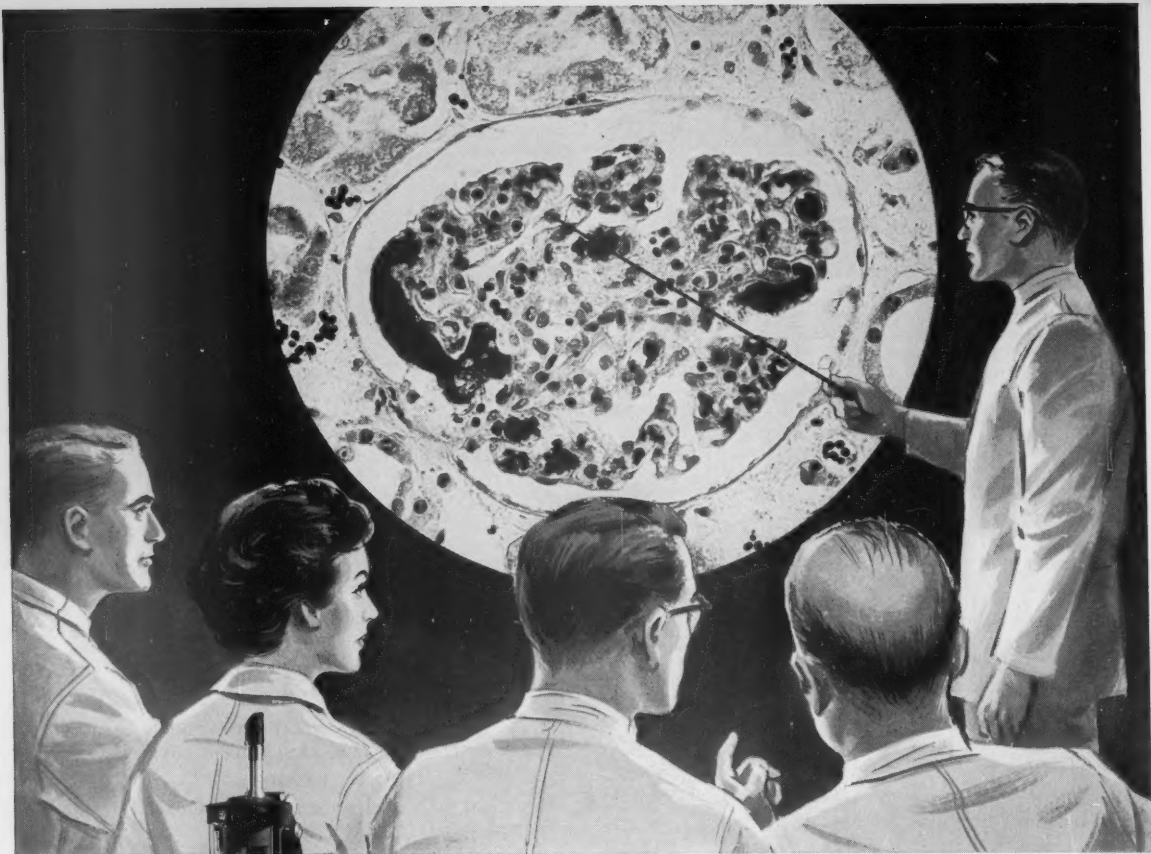
(own rate) But in an ordinary textbook the student is not \_\_\_\_\_ questions, nor are his successes \_\_\_\_\_, nor are his mistakes \_\_\_\_\_.

(asked, confirmed, corrected) James G. Holland and B. F. Skinner in their *The Analysis of Behavior*, published by McGraw-Hill, now offer a new kind of textbook that does offer these features. The book is, in effect, a machineless \_\_\_\_\_.

(teaching machine) The sequence of items that you are now reading is an example of the technique used in either a real teaching machine or in a \_\_\_\_\_ teaching machine.

(machineless) The new book makes for truly unforgettable reading, and we recommend that you \_\_\_\_\_ it.

(read).—J.T.



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## CURRENT PROBLEMS IN RESEARCH

# Molecular Basis for Action of Ionizing Radiations

A simple model describes the inactivation by ionizing radiations of molecules in the living cell.

Franklin Hutchinson

From an early date in its development, radiation biology has tried to give explanations in molecular terms of various phenomena observed. Indeed, in their attempts in this direction radiation biologists must be reckoned as pioneers in opening up the explosively developing field of modern molecular biology.

## The Target Theory

It was recognized early that certain simple biological systems, such as a suspension of bacteria, when irradiated, lost a measurable property—for example, the ability to multiply and form colonies—as an exponential function of radiation dose (see Fig. 1). Usually in these cases the effect was also found to be independent of dose rate. Such results were quickly correlated with a knowledge of the physical properties of ionizing radiations to produce the target theory of radiation action, as first propounded by Blau and Altenburger (1), Dessauer (2), Crowther (3), and Condon and Terrill (4).

The important characteristic of ioniz-

ing radiations in the target theory is the localized release of comparatively large amounts of energy, as graphically illustrated in the cloud chamber photograph shown in Fig. 2. Each water droplet represents the expenditure of 30 to 100 electron volts of energy, as may readily be determined by counting the number formed from the absorption of a known amount of radiation. Such an energy is large as compared to the energies of a few electron volts associated with even the strongest chemical bonds, and it is reasonable to assume that the immediate neighborhood of an ionization will be disrupted sufficiently to prevent the structure from carrying out a highly specific biological process such as an enzymatic reaction.

If the volume of a biological structure or target which must be intact to carry on a process is  $V$ , and the dose  $D$  is expressed in terms of primary ionization events per unit volume, then the mean number of inactivating events per target is easily seen to be  $VD$ . Some targets will receive a number of "hits" close to the mean number, others will receive more or fewer hits because of the random nature of the process. The most interesting class is that comprising the targets which have received no hits. The fraction of such targets is readily calculated from statistical considerations

to be  $e^{-VD}$ , and this relationship immediately provides a simple explanation for the exponential survival curve. The independence of dose rate follows from the all-or-nothing nature of the assumed mechanism.

A plot of the survival of more complex organisms as a function of dose is usually a sigmoid (so-called from its shape when plotted on linear graph paper) with a shoulder at low doses, as shown in Fig. 1. This is readily interpreted by a theory postulating either multiple targets or multiple hits in the same target. The target theory received its full expansion in two books which appeared just after World War II, *Actions of Radiations on Living Cells*, by D. E. Lea (5), and *Das Trefferprinzip in der Biologie*, by N. Timofeev-Ressovsky and K. G. Zimmer (6).

## The Diffusion Theory

Even as the target theory was approaching its prime, a second theory began to arise. An offshoot of nuclear energy studies after 1945 was the extensive development of the understanding of the radiation chemistry of water, a development sparked particularly by strong research groups at the various Atomic Energy Commission laboratories. It became increasingly clear that the action of ionizing radiation on water resulted in the formation of the highly reactive free radicals H and OH.



Since a living cell is 80 percent water, it is reasonable to assume that most of the absorbed energy will be used to form such water radicals, which can diffuse about the cell to produce other free radicals on organic molecules. These organic radicals again will diffuse before they form an even less reactive set of radicals, thus spreading the effects of the radiation further and further. This point of view received a tremendous impetus from the early work of Dale (7) and others (8),

The author is professor of biophysics, Yale University, New Haven, Conn. This article is based on a talk given 19 Apr. 1961 at the Western New York Nuclear Research Center, University of Buffalo.

Table 1. Variation in radiosensitivity (relative to that in the intact cell) of the enzyme invertase with stage of purification (31).

Stage of procedure	Radiosensitivity on purification by the method of		
	Dieu	Sumner	Fisher
In cell		1 ± 0.05	
Crude extract	1.48	1.43	0.83
Dialyzed extract	0.80		0.87
Precipitate	0.63		1.05
Final product		0.78	0.53

in which a dose of the order of a few hundred roentgens was found to destroy the activity of sufficiently dilute enzyme systems as effectively as it destroyed individual living cells. Clearly, the effects on dilute enzyme systems were entirely the result of diffusion of radiation-produced radicals, and the presumption was that the same process might occur also in cells.

Thus in a "diffusion" theory, as opposed to the "target" theory, radiation action was ascribed solely to the widespread diffusion of radiation-produced radicals. Specific phenomena of radiobiology, such as the effect of oxygen concentration and of various protective compounds, were interpreted in terms of changes in radical concentrations. This mechanism was sometimes referred to as "indirect action," as contrasted with the "direct action" underlying the target theory.

Although both of these theories describe experimental results in terms of molecular events, relatively little direct evidence, on the whole, was available for the mechanisms at work at the atomic level in the cell. Many workers, particularly D. E. Lea, saw the need for such data, but the largest single accumulation of data was inspired by a somewhat different viewpoint.

## Direct Action on Molecules

Ernest C. Pollard, at Yale, pointed out that with sufficient knowledge of the physical and chemical processes taking place, ionizing radiations could be used to study the living cell (9). This concept was foreshadowed by several investigators, notably Lea and Zimmer, but Pollard and his associates proceeded to amass a considerable number of the data necessary to make the idea a usable one (10).

Briefly, a large number of biological molecules were irradiated in the dry state with ionizing radiations. The survival of a specific biological property, such as enzymatic activity, was found to be exponential with dose, and independent of dose rate. From the slope of the survival curve, the target volume could be calculated. This required a knowledge of the energy needed to produce a primary ionization, which was taken to be 100 electron volts, the value deduced from measurements of ionization in gases (11). The use of this figure leads to a simple relation between the dose in rads (or roentgens) necessary to reduce activity to 37 percent of its initial value,  $D_{37}$ , and the mass  $M$  of the target volume, expressed in molecular weight units:

$$D_{37} \times M = 0.7 \times 10^{12}$$

It is clear that this relation predicts the result one intuitively expects—that a large dose will be needed to inactivate a small target, and vice versa.

Figure 3 illustrates some of the results. The known molecular weights of a number of molecules are plotted horizontally, and the equivalent molecular weights of the target volume, vertically. The straight line was drawn on the assumption that the two volumes are the same. The agreement over four

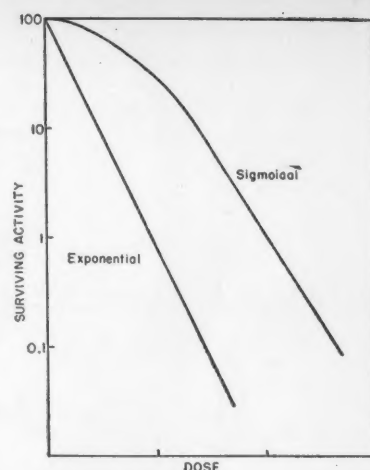


Fig. 1. Typical curves for the survival of biological activity, plotted vertically on a logarithmic scale against radiation dose on a linear scale.

orders of magnitude is impressive, and it is apparent that the target theory hypothesis is well supported.

The variations of the points from the line are larger than the experimental errors, showing that other factors are at work. The four points connected by a dashed vertical line are for the enzyme catalase at temperatures (reading from the bottom up) of  $-180^{\circ}$ ,  $20^{\circ}$ ,  $80^{\circ}$ , and  $112^{\circ}\text{C}$  (12). Another sort of change is shown in Table 1, in which is listed the radiation sensitivity of the enzyme invertase at various stages of purification from yeast cells. However, it is clear that the changes in the sensitive volume are of the order of a factor of 2. This corresponds to energy transfer over a distance only a fraction of the dimensions of the sensitive volume, so that the target concept is still essentially valid.

The basis for these results might still be questioned on the grounds that ionizing radiation produces large numbers of excitations, as well as ionizations. The question is, Why are these not counted in as inactivating events? However, Setlow (13) has measured the number of enzyme molecules inactivated per photon absorbed, or excitation produced. For most ultraviolet radiation, the yield stayed within the order of  $10^{-3}$  to  $10^{-2}$  even well down into the vacuum ultraviolet. However, for photon energies of the order of 10 electron volts, the yield increased sharply toward unity. Similarly, irradiating monomolecular layers of protein with very low

Table 2. Radiation doses needed to inactivate enzymes in cells (32).

Enzyme (cell)	Dose (Mrad) to reduce to 37% of original activity		Yield (in molecules per 100 electron volts) in dilute solution (G)	Diffusion distance $\rho$ (Å)
	Dry	Wet		
Invertase (yeast)	12	6	0.15	29
Alcohol dehydrogenase (yeast)	28	1.3	3.0	31
Coenzyme A (yeast)	200	3	2.7	35
Coenzyme A ( <i>E. coli</i> )		15	2.7	17
Coenzyme A (peas)		5	2.7	30
Coenzyme A (beef heart)		>100	2.7	<5
Coenzyme A (beef liver)		>100	2.7	<5
Acetylcholinesterase*	4.8	4.8		<0

\*See Cotzias and Serlin (33).

voltage electrons produced little loss in activity until the electron energy exceeded 10 electron volts, when the efficiency rose rapidly (14). In both these cases the presumption is that the removal of an electron is, for practical purposes, the effective event in biological action of ionizing radiations, and this justifies the use of 100 electron volts as the measure of the inactivating event.

The utility of this information for biological studies is very great. For example, one can use this method to determine the approximate molecular weight of a substance which has some specific assayable property. The unique feature is that the substance does not have to be purified in any way, since the measured radiation-sensitivity does not depend greatly on the surrounding medium, provided only that the substance be dried to prevent diffusion of water radicals.

The magnitude of the direct action on molecules such as enzymes in cells can be determined by the irradiation of dry cells. Table 2 lists the doses necessary to reduce the activity of some enzymes irradiated in dried cells to 37 percent of the original activity. The results are in good agreement with the target hypothesis, the larger enzymes (such as invertase) requiring lower doses than do small molecules such as coenzyme A.

If the cells are now irradiated in the normal wet state, the doses needed to inactivate drop greatly, as shown in Table 2, column 3. The most obvious assumption is that the diffusion of water radicals is contributing to the inactivation process. The relative proportions of the two processes, of indirect to direct action, can be seen to vary enormously from one molecule to another. For the first three entries, for different enzymes in yeast cells, for example, the ratio of dry to wet dose varies from 2 to 1 for invertase, to 20 to 1 for alcohol dehydrogenase, to 100 to 1 for coenzyme A.

#### A Simple Theory

This information can be fitted into a simple conceptual scheme in the following way. In the first place, different molecules have different sensitivities to inactivation by water radicals. Such sensitivities can be measured by determining the number of molecules inacti-

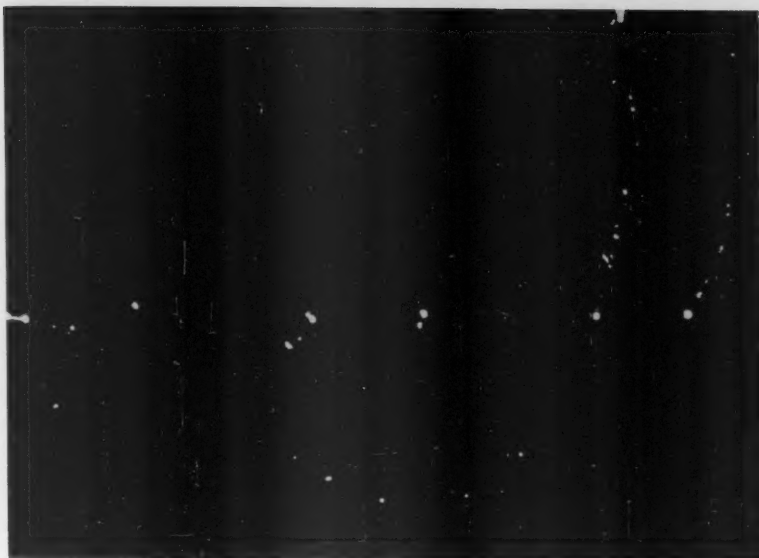


Fig. 2. A cloud-chamber photograph of ionizations produced by x-rays. [From P. Auger, *Ann. phys.* 6, 183 (1926), as reproduced from *An Atlas of Typical Expansion Chamber Photographs*, W. Gentner, H. Maier-Leibnitz, W. Bothe, Eds. (Pergamon Press Limited, London, 1954), reproduced with permission].

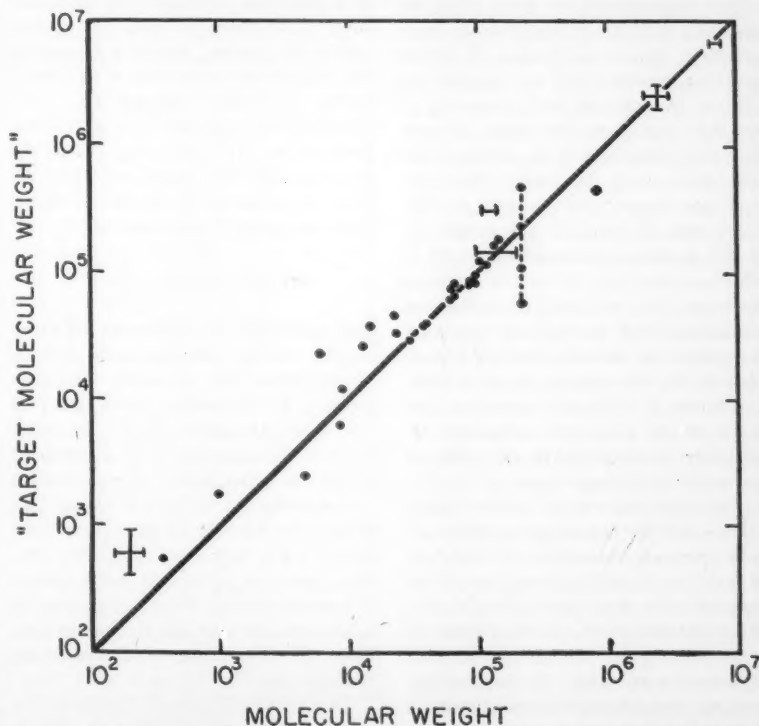


Fig. 3. The radiation target size, given in molecular-weight units for a variety of biological molecules irradiated in the dry state, plotted against the known physicochemical molecular weight. The straight line is the expected relation if the two molecular weights are equal. The data plotted are those given in Table 2 of E. C. Pollard *et al.* (10). The dashed vertical line connects four points representing the target size of the enzyme catalase at different temperatures (see text).

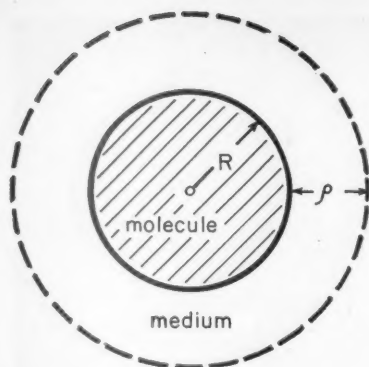


Fig. 4. A simple picture of radiation action on a molecule in a cell. The molecule, shown schematically as a sphere of radius  $R$ , is surrounded by a water layer of average thickness  $\rho$ . Water radicals from this water layer contribute to the inactivation of the molecule.

ated per unit dose delivered to a dilute solution, where the only process is the indirect effect. This yield  $G$ , in molecules per 100 electron volts of energy absorbed, is given in Table 2, column 4.

The requirement for large doses to inactivate enzymes in wet cells, as compared to the doses needed in dilute solutions, results from the removal of radicals by reaction with materials in the cell. Let  $\rho$  be the mean distance that the radicals diffuse through the cell before they disappear. Then, by a simple theory first worked out by Zirkle and Tobias (15), the magnitude of the indirect effect and the yield in dilute solution may be used to calculate the value of  $\rho$ , with only the additional assumption that the radical reacts on first encounter with the molecule being assayed. Values of  $\rho$  are listed in Table 2, column 5. The fact emerges that many of the measured values are remarkably constant and of the order of magnitude of 30 angstroms.

The assumption made in this calculation—that the radiation-produced radicals react on essentially all collisions with the target molecule—is reasonably supported by two lines of evidence. The most convincing is the recent set of measurements, by Harold Schwarz at Brookhaven (16), of the absolute reaction rates between hydroxyl radicals and  $H_2$  and  $H_2O_2$ . From these measurements and a number of previously determined ratios of rate constants (17) it can be determined that the probability that the hydroxyl radical will react with most organic molecules is

between .1 and 1.0. This value is in good agreement with earlier, less reliable, data obtained by a pulse technique (18). Since the calculated value of  $\rho$  depends directly on the square root of the probability, the change in the value of  $\rho$  will not be large.

The other evidence is that the observed radical diffusion distance is roughly the thickness of water which must surround the average macromolecule in a cell to account for the 80 percent of water included. The calculation here is one of order of magnitude only. From the known macromolecular composition of cells, the sizes of these molecules, and the known distribution of carbohydrate in cell walls and lipoproteins in membranes, we find that the average thickness of water in the cytoplasm is of the order of 15 to 50 angstroms about each macromolecule. The range of thicknesses reflects widely different assumptions about the ways in which the macromolecules are arranged.

The whole situation then reduces to the rather simple picture shown in Fig. 4. A particular molecule, shown as a sphere of radius  $R$ , will be inactivated if a primary ionization occurs within its volume. Radicals formed in the volume of water [equal to about  $4\pi R^2\rho(1 + \rho/R)$ ] immediately surrounding the molecule, will also cause inactivation. The efficiency will be determined by the measured yield  $G$ . Thus the effective inactivation volume, on a target theory basis, will be

$$4\pi R^2\rho G(1 + \rho/R) + \frac{4}{3}\pi R^3$$

The application to molecules of other shapes, such as long thin rods, follows directly from the discussion. The parameters  $R$  (molecular radius) and  $G$  (the yield for radical attack) are properties of the molecule, to be determined by suitable experiments. The parameter  $\rho$ , measuring the distance a radical can diffuse, is a function of the cell environment. It can vary from essentially zero for a molecule so located that it comes in contact with no water, as appears to be the case for acetylcholinesterase (see Table 2), to a value of the order of 30 angstroms.

Thus, it would appear that both the earlier theories are required to explain radiation action on a molecular basis and that a synthesis of the two appears to satisfy the experimental data. However, in essence the final result most closely resembles the target theory,

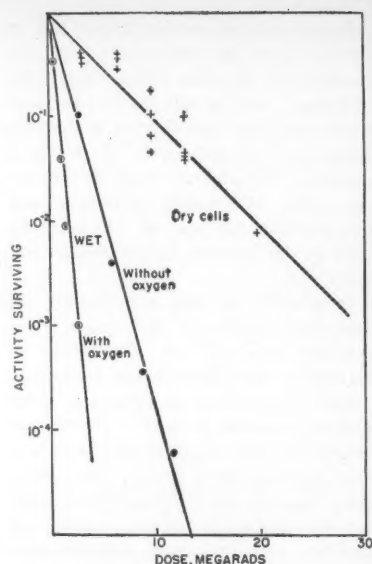


Fig. 5. The inactivation of a property (ability to transform) of DNA when irradiated under various conditions in a cell (21).

except that now the target has fuzzy edges.

The major point of this article has now been made. A large number of radiobiological data can readily be fitted into this scheme. There are also data which do not fit in so readily. Let us discuss a case which at first sight appears to be inconsistent but which, when the details are examined, is actually in complete agreement.

### Oxygen Effect in Cells

A well-established phenomenon in radiobiology is the ability of oxygen to increase the radiation sensitivity of a wide variety of living cells by a factor of 2 to 4 (19). This enhancement is so general that the most logical conclusion is that the process operates at the molecular level. Indeed, the radiation sensitivities of molecules in cells, such as the enzyme invertase in yeast cells (20) and the deoxyribonucleic acid (DNA) transforming principle in pneumococcus cells (21), are increased by a factor of about 3 in the presence of oxygen.

From the picture formulated it is clear that this increase must be either in the direct action, in the indirect action, or in both. An increased sensitivity in direct action—that is, enhancement of radio-sensitivity by about



a factor of 3 for materials in the dry state—has been demonstrated for a number of enzymes (22). However, the effect of oxygen on the indirect action of water radicals has been carefully measured for several enzymes in dilute solution (23), and only for a single one, deoxyribonuclease, has an enhancement with oxygen been reported. Deoxyribonucleic acid extracted from pneumococcus cells has been studied with extreme care in dilute solution (24). When a specific biological property of the DNA—the ability to transform (25)—was measured, no effect of oxygen on the radiosensitivity in dilute solution could be found.

Figure 5 shows that for DNA irradiated in pneumococcus cells, about one-third the total effect is presumably direct action occurring in dry cells, and that the indirect effect accounts for more than half the total inactivation in wet cells. Yet a full threefold increase in radiosensitivity is found in the presence of oxygen.

If the indirect effect does not increase in the presence of oxygen, then how is the oxygen effect on DNA in the cell to be explained? The answer is shown in Fig. 6. If compounds containing sulfhydryl groups, —SH, are added to dilute solutions of DNA or enzymes, the radiosensitivity is found to increase when oxygen is bubbled through the solution. This, of course, provides an interesting bit of information on the mechanism of the oxygen effect. In the present context, the significance is that since living cells contain sulfhydryl groups, the magnitude of the oxygen effect in vivo can be well correlated with the effects in vitro and there is no disagreement with the concept developed in this article.

#### Difficulties with Proposed Model

The model of radiation action that has been presented is so easy to visualize that it is too bad nature will not let us take it literally. Several well-verified experimental results show that certain factors have been left out.

**Change in direct effect with surrounding medium.** The data in Table 1 clearly indicate that the radiation sensitivities of dry molecules are a function of the surrounding medium. This could be the result of energy transfer into certain molecules, causing increased radiation sensitivity; energy transfer out,

to give protection; or changes in the physical state of a given molecule which make it more or less sensitive to a given amount of energy released within its structure. At the moment the effect is not an enormous one, but it would be worth while to try to understand the factors involved.

**The mechanism of the oxygen effect in direct action.** It has been assumed above that every molecule receiving a primary ionization is inactivated. The increase in radiation damage in the presence of oxygen is then hard to understand. Although other explanations are possible, the simplest is one given by Howard-Flanders (19)—that the actual number of primary events is higher than calculated and that only a fraction of them are manifested in the absence of oxygen. Whatever the true explanation, at least one more assumption will have to be added to the model suggested in this article.

**The variation in radiation sensitivity with temperature.** The radiation sensitivity of a number of enzymes in the dry state varies with temperature in much the same way that the sensitivity of catalase does (see Fig. 3). It is possible that this phenomenon, and the

two others also, involve energy transfer over distances of perhaps 10 to 30 angstroms. In the absence of accurate knowledge, the factors just discussed represent uncertainties of the order of a factor of 2 in the effects to be expected from a given dose of radiation.

#### Areas of Inadequate Information

Whereas these factors are known to complicate the simple picture, there are others whose importance cannot be determined because of lack of sufficient information.

**Change in the direct effect in the presence of water.** Since the direct effect does change with the nature of the surrounding medium, it is quite possible that the presence of water may change the response of a structure to an ionization within it. Closely related to this is the result of energy release in water molecules which are firmly bound to a macromolecule. There are some indications that these considerations are important. Okada (26) has found that the yield (number of molecules inactivated per 100 electron volts of energy absorbed) drops when an equal mass of water is absorbed onto a dry enzyme preparation. It has also been reported that the degradation of polysaccharides is less efficient in the presence of a small amount of water than in the dry state (27). Suitable experiments to measure any change in direct effect with hydration are badly needed.

**Energy required per primary ion cluster.** The figure of 100 electron volts which has been used for energy required per primary ion cluster was obtained from gas data only. Recent considerations have cast doubt on the validity of using gas data for effects taking place in condensed (liquid or solid) phases. On the experimental side, modern techniques (28) have made it possible to pass a monoenergetic beam of 5- to 20-kilovolt electrons through a foil so thin (approximately 100 angstroms) that the average electron makes only a single interaction, and to analyze, in energy, the transmitted beam with sufficient accuracy to detect losses of even an electron volt or so. A typical curve of numbers plotted against energy loss is shown in Fig. 7. The analyzers used so far for these purposes accept electrons only within a very narrow angle of scattering, so that the total

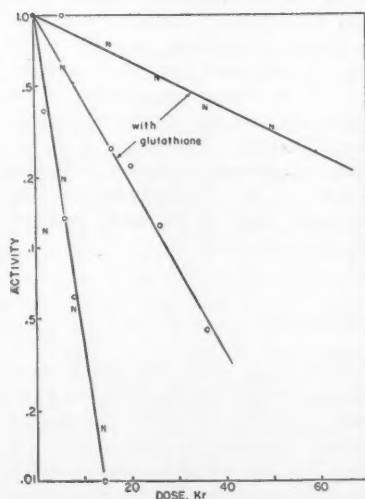


Fig. 6. Inactivation in dilute solution of the ability of pneumococcal DNA to transform. The steep curve to the left shows that inactivation is the same when the irradiation is carried out under a nitrogen (N) or an oxygen (O) atmosphere. When glutathione is added, the decrease in sensitivity is caused by a relatively trivial event, the removal of water radicals by reaction with glutathione. The significant point is that the radiosensitivity is then different in oxygen and in nitrogen (23).

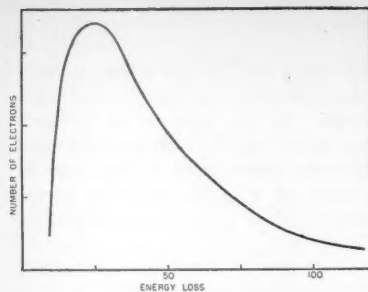


Fig. 7. A typical plot of number of electrons against the energy (in electron volts) lost by the electrons in passing through a very thin plastic foil (28).

number of electrons losing a given amount of energy can be determined only by summing data over many angles.

The data obtained reveal two interesting facts. One is that in solids very few electrons lose an amount of energy between 2 and 10 electron volts, whereas in gases losses of energy (corresponding to excitation of molecules) in these amounts are the most probable loss events. Second, from crude data taken on Formvar films and integrated over all angles, it appears possible that the mean energy loss per interaction event may be considerably smaller than the 100 electron volts determined from the gas data.

On the theoretical side, in a recent paper Fano (29) has proposed a possible explanation of both these effects, based on the mutual interaction of excited states of molecules which are located sufficiently close together, as in the solid state. Better understanding of this matter, and particularly a reliable value for the mean energy per primary interaction event, is clearly needed. Experiments along these lines are underway at present.

**The fate of the ejected electron.** In direct action, an almost mystical significance is ascribed to the act of ionization—that is, the actual separation of an electron from the parent molecule. This significance is based on sound enough reasoning, since the vacuum ultraviolet and the very low energy electron experiments both tend to indicate a rapid rise in inactivation efficiency as available energy passes the level of ionization energy—about 10 electron volts for many organic molecules. A better understanding of why this is so probably hinges on knowing what happens to the ejected electron.

In indirect action the ejected electron

is usually believed to interact with water in some way to form the species customarily referred to as the H atom. The spatial relationships of the OH and H radicals at formation are hotly in dispute at the moment. If the electron returns to the parent ion, as some maintain, the OH and H radicals will be formed close together, and probably in about the same yields within the cell and in dilute solutions. On the other hand, if the electron wanders away from the ion, it may be captured 10 to 100 angstroms away from the OH radical formed near the positive ion. In fact, in the cell it may not even be captured by a water molecule, but may be captured by part of the solid phase, so that few of the species classed under the name "H radical" would be formed at all in the cell.

The biological effect of any low-energy free electrons formed either from water or from the direct effect is also of interest. The one bit of information available about this is that electrons of energies below 10 electron volts, as mentioned before, seemed to have very little effect on protein monolayers (14).

Over and above these points there is the consideration of the basic mechanism of inactivation. If the target volume is the whole molecule, does this mean that all of the molecule is necessary for a specific biological action, or is energy transferred into the active site? If the latter supposition is right, why is the energy transferred to the active site and not to some unessential part? Possibly a knowledge of the effects of ionizing radiation will contribute to an understanding at the molecular level of the whole problem of biological specificity.

## Conclusion

While it is clear that much more needs to be known about detailed processes, it seems likely that the general picture presented in this article will provide a convenient framework within which to order many of the phenomena treated in radiobiology. Not only does this picture incorporate many of the concepts found useful in earlier theories but it also has the value of being simple, concrete, and easily visualized. From the theory, a reasonable estimate may be made of the effect of a given dose of radiation on a specific kind of molecule in a cell. Conversely, from the immediate effects produced by a certain

dose, some estimate may be made of the mass of intracellular material which must be involved in the processes which are assayed for. Perhaps these advantages will suffice to carry the theory over its many difficulties and deficiencies until another and more encompassing viewpoint can be reached (30).

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# Report on Russia: Geochemistry and Politics

Soviet geologists are busy with a host of projects,  
but in their off-hours they enjoy talking politics.

Konrad B. Krauskopf

During March of this year I was privileged to spend three weeks in the Soviet Union as a visiting scientist, for the purpose of exchanging views on education and research with Russian geologists and geochemists. By good fortune I had also an exceptional opportunity to learn something about the attitude of my Russian colleagues toward world problems.

My itinerary took me to the universities and institutes of the Academy of Sciences in four cities: Moscow, Leningrad, Kiev, and Tashkent. Nearly everywhere I was received with the greatest cordiality, and was able to see laboratories and talk freely about current research problems. The talk often strayed beyond scientific subjects to politics and world affairs, and with the aid of an extremely able interpreter I found it possible to explore such extracurricular matters in great detail. The interpreter, a geologist with an enviable command of idiomatic American speech, was himself much concerned about social questions and was eager to give me all possible opportunities to correct my misconceptions about his country and to learn the viewpoints of Russian scientists. Some of these viewpoints are worth reporting, since they represent the thinking of an important group in Soviet society.

In these pages, therefore, I shall summarize briefly the current status of geochemical work in Russia—greater detail is hardly warranted, since the subject has been discussed elsewhere (1)—and then describe, I hope objectively, some of the opinions of Russian geologists regarding current relations between their country and ours.

## Geochemical and Geological Research

My geological and geochemical colleagues were for the most part very cooperative in exhibiting their laboratories and in discussing research projects. These subjects are not politically "sensitive," so there was no reason to expect secretiveness, but I was nevertheless pleasantly surprised at the lack of hesitation in bringing out field maps and rock specimens and in discussing details of research techniques. Americans often complain that published geologic work by Russians is annoyingly vague about exact locations and scales of maps and about experimental details, but there was little vagueness in our conversations.

Geology in general is an active field of science in present-day Russia. Mapping is in progress in many parts of the country, under the supervision of the Ministry of Geology (an organization analogous to the U.S. Geological Survey, but lacking the Survey's extensive research activities), aided during the summer season by personnel from the universities and academies of science. Geologic mapping on a scale of 1:250,000 will soon be completed for the entire country, I was informed, but these maps are not available for public sale. Russian geologists express the same sense of excitement about the little-explored areas of Siberia and Central Asia that American geologists felt about our Far West a generation ago. These are the lands of the future, they say, lands full of fascinating geologic problems and abounding in mineral wealth, the discovery of which has only just begun.

The special field of geochemistry

has a long and honored tradition in the Soviet Union, since two of the pioneers in the modern development of the subject, A. E. Fersman and V. I. Vernadsky, were Russians. Active research is under way in most branches of the field, the kinds of problems and methods of investigation being very similar to those in the United States. Two sorts of problems receive special emphasis: the development of methods of prospecting by analyzing soil, water, and vegetation for trace elements and the use of geochronometric methods based on radioactivity for answering questions about stratigraphy and structure. In almost every institute I visited, laboratories of geochemical prospecting and geochronometry were in operation.

The laboratories I saw were well equipped with modern instruments. Requests for instruments, I was told, are seldom disallowed, but procuring of the equipment may be subject to long delays. Overcrowding is serious in some of the laboratories, but everywhere the provision of more space for scientific work has a high priority in the building program. Especially worthy of note is the number of laboratory assistants and technicians, the latter including highly trained analysts, physicists, and electrical engineers.

Research activity is scattered among many institutions. Most research in geological fields is concentrated in the Academies of Sciences, organizations that have no real counterpart in America. Perhaps the various laboratories of the Carnegie Institution provide the closest analogy, but the Russian academies are supported by the government rather than by private funds and are responsible to the government. Academies or branch academies are located in most of the principal cities, the largest and most famous being the National Academy in Moscow. Each academy is divided into institutes specializing in particular fields of science, the number and character of the institutes varying from city to city in accordance with local needs and interests. Both practical and theoretical research projects have a place in the academics, the emphasis being more on practical work in the academies of outlying cities and on theoretical research in Moscow. Besides the institutes of the academies, there are a number of independent in-

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stitutes engaged in geological research, mostly of a practical nature.

Universities in Russia are primarily institutions for teaching, but good facilities are available for training students in research techniques and for considerable research by faculty members. Geological research is stressed particularly at the State University in Moscow. Faculties in geology at the universities are large, and instructional equipment is good. My contacts with students were limited, but on the basis of a few conversations I judge that the quality of the professional education in the four schools I visited is comparable to that in good American institutions. Close cooperation between the universities and academies of science is the rule, professors often holding dual appointments and advanced students being permitted to work in academy laboratories.

This scattering of research activity aroused my curiosity about problems of coordination. In response to queries I was told that coordination of research is handled by committees, and that the work of the committees is generally satisfactory. Issuance of the recent decree on reorganization of research, however, suggests that coordination is indeed a serious problem, at least in some fields of Russian science. It seems likely that henceforth the academies will devote themselves more exclusively to basic research and that practical investigations will be left to the specialized institutes (2).

The best equipped and best staffed laboratories are those of the academy in Moscow, as might be expected, but even in a spot as far off the beaten track as Tashkent the amount of modern laboratory apparatus is most impressive. Two institutes of the Academy in Moscow are particularly noted for the amount and excellence of their geochemical work, the Vernadsky Institute of Geochemistry and Analytical Chemistry (A. P. Vinogradov, director) and the Institute of the Geology of Ore Deposits, Petrography, Mineralogy, and Geochemistry (F. V. Chukhrov, director). Examples of current geochemical projects at the two institutes are given in the accompanying box (page 541). Several other institutes of the Academy in Moscow are engaged in geochemical work, notably the Fersman Museum, the Institute of Rare Metals, the Institute of Hydrogeology, and the Institute of Oceanography.

In Leningrad the principal field of geochemical interest is geochronometry. E. K. Gerling, chief of the geochronometric division of the Laboratory of Precambrian Geology, is the recognized Russian authority in this field. In Kiev most of the geochemical effort is directed toward problems of interest to the Ukraine—ages of the Precambrian rocks, origin of the iron and manganese deposits, and geochemical prospecting. In Tashkent, likewise, most attention is given to problems of local interest, especially the composition and movement of ground water and the origin of loess, but laboratories are being set up for work on more theoretical problems such as the distribution of stable isotopes and high-temperature reactions of silicates.

What sort of assessment can one make of the Russian geochemical effort as a whole? Any generalization of this sort is dangerous, especially when it is based on such brief observation. The amount of work is impressive: tremendous numbers of young scientists have been drawn into this rather specialized field, and geochemical papers appear in great profusion. Some of the papers are remarkably good, but perhaps the sheer number of workers makes the average quality of the product seem mediocre. To an outsider, a disproportionate amount of the Russian work appears to be of the empirical, fact-gathering sort, without much imaginative insight into the reasons for gathering the facts or into the meaning of the facts once gathered. This may well be the result of training so many people so fast; it may also be the kind of geochemistry that is most needed at the moment in a country where geological exploration is only now getting under way. Certainly I think an American can say, without meaning to be boastful and without in any way disparaging the best Russian papers, that no Russian laboratory so far can point to a record of consistent, long-continued excellence in research comparable to the records of a few laboratories in this country. Very likely this is only a question of time. With the good equipment available, the numbers of assistants, the rigorous university training, and the widespread public enthusiasm for science, geochemical research in Russia during the next few years should have every opportunity to become the equal of the best research elsewhere in the world.

## Political Views of Russian Geologists

Geologists in Russia are no more experts on political and social questions than geologists in America, but like their American colleagues they have strong opinions which they enjoy talking about. It was my good fortune to hear many of these opinions expressed under very informal circumstances, in conversations that grew out of scientific discussions in the laboratories. All in all, I must have discussed political and social questions with nearly two dozen geologists and geochemists. These conversations, either with individuals or with groups, and interlaced with scientific matters, ranged from brief exchanges to sessions that were continued far into the night in Russian homes.

Neither the Russians nor I had any idea at the time that these impressions would ever be written down, so the paragraphs that follow are not to be considered as accurate opinion sampling. The Russian views seemed in many ways startling, for they represented the thinking of men with the same professional background as my own, reasonable and well-educated men who have made an honest effort to examine the issues that divide our troubled planet, and who have arrived at conclusions diametrically opposite to those that a Westerner thinks self-evident.

Underlying the world view of my geologist friends is a deep enthusiasm for communism. In part this is an expression of gratitude for benefits received: many geologists have come from humble origins, and say proudly, "I am the son of a worker," with the implication that only under communism could a worker's son rise so high. But the enthusiasm has deeper roots than this. In large measure it is a sense of mission, of dedication to a great cause, of being part of a progressive movement that will make the world a better place. The ideals of communism, however much we in the West think of them as perverted by an oppressive dictatorship, live on in the minds of these scientists. The Great October Revolution is as much a source of inspiration and a guide to action for these geologists as the American Revolution has been for us.

To a Western observer the enthusiasm seems hardly justified by the material rewards that communism has brought to the Russian people. The drabness of life in the Soviet Union—the unimaginative clothing, the monot-



## Examples of Current Projects at Two Institutes of the National Academy of Sciences in Moscow

### Vernadsky Institute

A. P. Vinogradov: radiocarbon dating; sulfur isotopes; geochemistry of tungsten; titanium content of bauxites; chemical evolution of the earth.

N. I. Khitarov: reactions at high temperatures under hydrothermal conditions; solubility of water and carbon dioxide in silicate melts; pressure-volume-temperature relations in the system  $H_2O-CO_2$ ; conditions of formation of zeolites.

A. I. Tugarinov: geochronology; lead isotopes; ratios of rare-earth metals and hafnium-zirconium in minerals and rocks.

G. P. Malyuga: geochemical and biogeochemical prospecting.

A. B. Ronov: distribution of rare metals in sedimentary rocks of the Russian platform; paleochemical maps; geochemical history of atmosphere and hydrosphere.

V. V. Scherbina: behavior of trace metals in the weathering zone; concept of acidity in silicate melts.

V. L. Barsukov: geochemistry of tin and boron.

### Institute of the Geology of Ore Deposits

F. V. Chukhrov: occurrence and mineralogy of clay deposits.

D. S. Korzhinsky: theoretical thermodynamics, especially thermodynamics of open systems; thermodynamics applied to magmatic processes, metamorphism, and ore deposits.

I. I. Ginzburg: geochemistry of weathering; origin of laterites and bauxites; geochemical prospecting.

A. A. Saukov: geochemistry of mercury; prospecting for metals and oil.

G. D. Afanasiev: geochronology, igneous rocks, and ore deposits of the Caucasus.

A. A. Ostrovsky: solid-state phase relations at high temperatures and pressures.

G. S. Gorshkov: geochemistry of volcanic exhalations in Kamchatka and the Kuril Islands off the coast of Japan.

L. N. Ovchinnikov: ore deposits of the Urals; hydrology of northeast Siberia.

onous food, the inadequate housing, the crowded stores with dull show-window displays—is remarked by every tourist from the West. There was no argument on this point by my geologist friends; they know enough of the West, either through personal visits or through conversations with foreigners, to realize how low the Russian standard of living is by comparison. Their reaction was simply that a low living standard is not important as long as conditions are improving. "Look at the primitive conditions we started from," they insist. "Remember that only recently we fought a disastrous war in which much of our land was overrun by the enemy. We have made great strides already, and now progress is visible from month to month, almost from day to day." The feeling of steady improvement, the joy of seeing more and more goods available in stores, the satisfaction of watching apartment houses materialize almost overnight, are enough to nurture enthusiasm despite present scarcities.

An important ingredient in the world outlook of Russian scientists is the idea that their government has given them freedom in large and increasing measure. This attitude came as a shock to my Western ears, so long accustomed to hearing the West

described as the "free world," in contrast to the "slave world" of the Communists. Far from acting like slaves, my Russian acquaintances boasted of their freedom, maintaining even that in some respects freedom under communism is superior to that in the West. They seemed genuinely puzzled by the assurance of Westerners that true freedom exists only outside the Soviet world. The confusion arises in large part from a difference in usage of the word *freedom*—or more precisely, a difference in the kinds of freedom that seem particularly important on the two sides of the Iron Curtain.

Perhaps uppermost in the minds of my Russian acquaintances when they speak of freedom is freedom of opportunity—opportunity to get an education and then to work at a job and in a place of one's own choosing. Every Russian, I was repeatedly told, as part of his elemental rights is guaranteed a free education up to the limit of his abilities—and the opportunity does not depend on the size of his father's fortune or the color of his skin. If a Russian is trained in a profession he is expected to work for a few years in that profession (this seems reasonable inasmuch as the state has paid for his schooling), but sub-

sequently he can change employment as he wishes. His opportunity to move to another job in another city is limited only by the scarcity of housing, which in some parts of the country is still acute.

Freedom from fear of arbitrary arrest is another blessing that my friends rated very high, perhaps especially high because it is a freedom that has come to the Soviet Union only recently. Political prisoners have been released from the notorious Siberian camps, I was told by two geologists who have worked in Siberia, and the camps are now used only for common criminals. Two geologists went so far as to maintain that Soviet law ensures greater protection for individual rights than do the laws of Western nations. What measure of truth there is in these assertions I will not here attempt to judge, but they are articles of belief among Russian scientists.

Freedom from another kind of fear, the fear of economic insecurity, has been very largely attained in Russia, I was told, for the government guarantees employment, medical care, and old-age support. So accustomed are my friends to regarding continuous employment as a basic right of every citizen that they find unemployment in Western states hard to comprehend.

"How can a country as rich and powerful as the United States permit six million people to be unemployed?" I was often asked. Joblessness in the eyes of these Russians is a relic of barbarism, something that excites the same sort of physical revulsion that we in the West feel when we read about arbitrary executions in Communist lands.

That freedom of speech now exists in Russia is amply attested by our conversations, which were held in public places as well as private, and always without the slightest show of apprehension. My friends were candid in admitting that a few years ago such conversations would have been impossible, and they point to this relaxation as a sign of the progressive nature of the Soviet regime. A Russian is still not permitted to publish articles critical of the government or to make critical speeches, but in private conversations he may express his views freely, to foreigners as well as to fellow Russians.

One area of freedom in which a Westerner can claim real superiority is that of ability to obtain information. A Westerner can read in his own language, as his Russian colleagues cannot, critical discussions of important issues from many points of view. The Russians hear the Western viewpoint only from broadcasts by the BBC and the Voice of America, to which they are now permitted to listen—another relaxation of recent years. Otherwise, in newspapers and magazines, they are limited to news as it is sifted and interpreted by their government and by Communist governments elsewhere. My acquaintances admitted readily that this is a kind of freedom about which the West can justifiably boast. They explained its absence in their country on the grounds of political inertia: in the past, when Russia was weak, restrictions on outside information were necessary; now that the country has become strong the restrictions should be lifted, but politicians are slow to change their ways.

Freedom to choose candidates for public office should, seemingly, be another place where the Westerner would have the better of the argument, but this proves to be a difficult subject to discuss because words are used in different senses. It is almost impossible, for example, to explain to a Russian what "free election" means. "How can you call your elections 'free,'" he will ask, "when no candidate can get his name on the ballot unless he has pow-

erful financial backing, and when the opinion of the electorate is molded by the expenditure of incredible sums for radio and television broadcasts?" In Russia, he will explain, candidates are discussed openly and thoroughly in meetings of the local soviets; once a candidate is selected by this process and is approved by the Party, the electorate rallies behind him and gives him the 99-percent majority which always seems so ludicrous in American eyes. My acquaintances seemed quite sincere in regarding this way of choosing candidates as actually more democratic than the American method.

In all these many aspects of freedom, Russian geologists find only a few areas where they concede superiority to the West, and these, they feel, are balanced by the areas where their own brand of freedom is more extensive. Very probably, of course, members of other professions—artists and writers, for example—would feel the Communist restrictions on freedom more acutely. But it seems important to note that, for at least one group of educated Russians, life is full and satisfying under the Soviet system, so much so that the Western variety of freedom has little attraction for them.

When our talk turned to the relations between Russia and the rest of the world, a sharp difference in the image that each side holds of the other made discussion difficult. The Westerner regards the Russians as controlled, for the most part without their knowledge, by an oligarchy of rapacious and malevolent men who seek constantly to foment world revolution. The Russian is equally convinced that the West (which means really America, for in Russian eyes all other Western countries are American satellites) is being victimized by a small group of profit-mad "monopolists" who pull the strings that control government, press, and radio and who try to instigate wars in order to sell munitions. On the level of informal conversations such as ours it was impossible to resolve this difference in viewpoint. Each of us was repeating what he had read in his own newspapers, and each was suspicious of the other's sources.

The contrast in our images of each other became particularly evident when we discussed parts of the world where communism and capitalism are currently in sharp conflict. In southeast Asia, for example, my geological friends picture their country as the

defenders of the workers and peasants against corrupt ruling classes who have exploited the people mercilessly for thousands of years. The Soviet Union is not intervening but is only sending materiel and advisers to the people's armies to counter the military aid which Western monopolists give the exploiters in order to protect their investments. If I objected that the West also is interested in the people's welfare, I was met by queries as to why we then support petty dictators, and why American monetary aid always finds its way into the pockets of the wealthy classes. If I maintained that the West was trying to preserve the people's freedom, I was taunted with the old questions, "Freedom for what? To live in abject ignorance and hopelessness? To have their labor exploited for another five thousand years?" If I suggested the desirability of free elections, the answer came back: "How can there be free elections when the people are ignorant and their votes will be bought by the exploiters?" My acquaintances seemed to have no doubts of the benign intentions of their government, or of the evil purposes of the capitalist nations—just as we in the West see only noble motives in our own governments and nothing but evil in the Communist leadership.

Except for their suspicions of our government and especially of supposed unscrupulous financiers behind it, the Russians I talked with were uniformly well disposed toward Americans. They genuinely admire our high standard of living, our efficient industries, and our scientific accomplishments. They are eager for scientific exchanges and scientific cooperation with Americans. Many times I heard the wish expressed that our governments could patch up their differences so that Russians and Americans could get better acquainted. Russian geologists share the convictions of their leaders that communism will eventually dominate the world, but for the present they see no reason why communism and capitalism should not exist side by side in peaceful competition. Above all, they do not want war. It is ludicrous, or tragic, or terribly frustrating, according to one's mood, to hear a Russian scientist say fervently: "How happy the world could be, if only America weren't so belligerent!"

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# Science and the News

## Grand Strategy: The Views of the Administration and the War College Do Not Seem To Coincide

A running debate has been going on in the Senate for nearly a month now over the Fulbright memorandum drawing the attention of the President and Defense Secretary MacNamara to what Fulbright sees as the excessive involvement of the military in politics. The bulk of Fulbright's memorandum, and all of the debate thus far in the Senate, has concerned itself with the tendency of "strategy seminars" and similarly named public education programs, sponsored or cosponsored by military organizations, to go beyond their stated purpose of alerting the public to the menace of the cold war to include speakers and literature which condemn large parts of the Administration's domestic program, such as federal aid to education, as steps toward socialism, which, in turn, is defined as merely a step toward communism. The military involvement in such programs has been based on a directive signed by then President Eisenhower in 1959 instructing the military to play a role in alerting the public to the menace of the cold war. Fulbright suggested that the Eisenhower directive, aside from the way it has been implemented, was a "basic error." "The American people have little, if any, need to be alerted to the menace of the cold war," he said. "Rather, the need is for understanding of the true nature of that menace. . . . There are no reasons to believe that military personnel generally can contribute to this need beyond their specific technical competence to explain their own role. On the contrary, there are many reasons, and some evidence, for believing that an effort by the military, beyond this limitation, involves considerable danger."

In answer to this Senator Thurmond, of South Carolina, the States' Rights candidate for President in 1948, has been making a series of speeches arguing, quite bluntly, that the programs

are fine, and that the fuss over them is just a reflection of the liberals' annoyance at having the truth told about where their policies are leading, and, occasionally, that the campaign against military informational programs is, at heart, communist-inspired. Thurmond has been supported by Senator Goldwater and, in more restrained language, by Mundt and Case of South Dakota. Thurmond demanded that the Senate Armed Services Committee investigate the whole business, but Senator Russell, of Georgia, the acknowledged leader of the Southern conservatives and chairman of the Armed Services Committee, has thus far ignored the request.

What is curious is that this debate over occasional right-wing activities of the military has drawn attention away from another, equally interesting, side of the Fulbright memorandum, which was concerned with the relationship of the Joint Chiefs of Staff and the National War College with three closely tied organizations: the Institute for American Strategy, the principal sponsor of many of the strategy seminars Fulbright complains about; the Foreign Policy Research Institute at the University of Pennsylvania, which produced the basic text *American Strategy in the Nuclear Age* for the Institute for American Strategy programs; and the Richardson Foundation, a source of financial support to both. Fulbright asked that the relationship between these organizations and the Joint Chiefs and War College be "re-examined from the standpoint of whether these relationships do not amount to official support for a viewpoint at variance with that of the Administration" and whether this relationship "may give one particularly aggressive view a more direct and commanding influence upon military and civilian concepts of strategy than is desirable."

None of these organizations advocate the extreme right-wing views that frequently are presented at the strategy

seminars; indeed they officially advocate no particular view of domestic political questions, since their concern is with foreign policy. Extreme right-wing views have occasionally set the tone of the Institute for American Strategy seminars, but this apparently is not so much because such views represent the views of the Institute—indeed they conflict on such questions as foreign aid and cultural exchange programs—but because the basic foreign policy views of the Institute have so far won little support except from the far right, and the sponsors of the program are in no position to offend the followers of Senators Goldwater and Thurmond, without whom they would have virtually no politically active support at all.

There is, in any case, a feeling within the Institute that even if domestic welfare programs are not objectionable in themselves, their expansion draws resources away from the massive expansion of the defense budget which the Institute views as the real need. Thus, for the Institute, the far right is at once a source of political support, a source of speakers with a suitably hard line on communism, and a source of opposition to the tendency to expand domestic spending, when, in the view of the Institute, we are, essentially, at war, and the need is for expanding defense spending.

### The Forward Strategy

Since 1945 research institutes in foreign policy questions have been organized at about a dozen major universities, and of these the most curious is the Foreign Policy Research Institute, which, much more than other such groups, has set itself the task of developing and promoting the acceptance of a specific strategic doctrine. This is called "the Forward Strategy," and its basic premise is that Democracy and Communism are locked in a struggle to the death, to be resolved only in the destruction of one side or the other; that the communists have wholly committed themselves to win this struggle by any means, preferably short of but if necessary by nuclear war; and that the Western democracies, led by the United States, will probably lose this struggle unless we, too, wholly commit ourselves to victory, by any means, and at any price. As defined in the Institute's *A Forward Strategy for America*: "The priority objective of any American grand strategy is, by a broad margin, the preservation and enhancement



of our political system rather than the maintenance of peace. . . . Our policy must be based upon the premise that we cannot tolerate the survival of a political system which has the growing capability and the ruthless will to destroy us. We have no choice but to adopt a Catonic strategy." "Catholic strategy," of course, derives from Cato's dictum, "Carthage must be destroyed."

The Institute sees the relative readiness of East and West to commit themselves to this Catonic strategy as a test of the intrinsic worth of the men produced by the rival systems: "If the communists prove to have more courage, a stronger will, a more steadfast spirit, a clearer intellectual insight into conflict in the nuclear age, they obviously are the better men and deserve to win—and probably will."

### Strategic Considerations

The program recommended by the Institute involves an expansion all along the line of programs related to the cold war, including such things as economic aid and cultural exchanges, all of which are to be moved by a guiding philosophy which regards all as weapons of war. But the principal element is a prompt expansion of the military budget, to perhaps \$65 billion a year, to the point where we would have the power to win a clear victory over the Russians in a nuclear war even if the Russians should strike first with a surprise nuclear attack. With this clear military superiority, we would proceed to beat down the Russians, most directly, one gathers, by fomenting revolts in the iron curtain countries, perhaps within Russia itself, and moving in with our troops if the Russians should try to intervene. We would intervene regularly in countries where the communists have fomented guerrilla warfare, using, the book suggests, tactical nuclear weapons. What if the view of the Administration should prove correct and it is impossible, or at least impractical, to build our military forces to such overwhelming superiority to the Russians that we would win a clear victory even after a Russian first strike? The book is vague on this, but it is a very important question, for if we lack an overwhelming superiority in military strength, there are limits to how aggressive our cold-war policies can be, since the Russians would presumably at some point react as we have on the question of the freedom of West Berlin and simply insist that the limit

is being reached. At this point the Catonic policy breaks down, for it becomes not only a policy of destroying your enemy, but of destroying yourself as well. The Forward Strategy does not discuss this problem, and in fact is quite hazy in general when it comes down to the specifics of putting its policies into action. Indeed, in some chapters of the book the Catonic policy seems to be abandoned in favor of leaving open a hope for a gradual lessening of tensions. In part, this may derive from the book's diversity of authorship: the title page lists three principal and eight subordinate authors. In part it appears to derive from the same source that makes for vagueness and occasional inconsistency in political platforms: the book is written not merely to present a strategic doctrine as an intellectual exercise, but to win support for the doctrine, and there is consequently the temptation to put in a little something for everyone who might possibly be won over. But in large part, the haziness appears simply to reflect the fact that certain things cannot be stated very bluntly in public. For the message emerges clearly, even though it is never clearly stated: that we may not be able to gain the absolute nuclear superiority that might give us the power to effectively force a Russian surrender without resorting to nuclear war, but that during the 1960's we do have the ability to build a preponderance of nuclear power to enable us to win, in the authors' view, a satisfactory victory in a nuclear war, provided we strike the first blow. The winner of such a war, the authors have told us, would then be in a position to "subject to his writ the entire world."

### First Strike

The authors point out that we have rejected a strategy based on a surprise attack, but hastily add that this could always be changed *almost to the last minute* (their emphasis). Indeed, say the authors, "even at the moment when the United States faces defeat because, for example, Europe, Asia, and Africa have fallen to Communist domination, a sudden nuclear attack against the Soviet Union could at least avenge the disaster and deprive the opponent of the ultimate triumph. While such a reversal at the last moment almost certainly would result in severe American casualties, it might still nullify all previous Soviet conquests."

The strategy endorsed by the book emerges as one of building our armaments as high and as fast as we can

during the limited time when we still have a far stronger economic base than the Russians and while the U.S. and Russia remain the only two powers with major nuclear striking forces; to push the cold war, in all phases, as aggressively as possible; and sometime before the Russians feel strong enough or desperate enough to launch the first attack themselves, to strike a surprise knockout blow and, presumably, proceed to "subject to our writ the entire globe," thus making the world safe for democracy. This policy is not specifically stated in the book: it is merely the only realistic policy that follows from the premises of the book, and the members of the Foreign Policy Research Institute consider themselves, above all else, as realists.

This, of course, is a quite different strategy than the Administration seems to have in mind, which accepts neither the basic premise that the conflict can be resolved only by the destruction of one side or the other, nor the assumption that this Catonic strategy would really be a constructive step toward shaping the kind of world we wish to live in. Nevertheless, the Institute for American Strategy has so far been able to operate its public-information programs under an aura of government approval, and the Foreign Policy Research Institute, until very recently, at least, has been the principal adviser to the National War College on the global politics courses given to promising young officers.

The most recent major Strategy Institute conference, for example, was the 7th annual National Military-Industrial and Educational Conference, a 4-day meeting in April this year devoted to the necessity for improving teaching in schools regarding the dangers of Communism. The program announced that the conference was being held "under the auspices of the Institute for American Strategy in cooperation with the U.S. Department of Health, Education, and Welfare." According to a spokesman for HEW, the department's role was limited to giving permission, before the change in Administration, to use its name in what seemed a good cause. The program also contained a routine message of greeting from President Kennedy, such as the White House sends out on request to almost any reasonably prominent gathering that requests one. This conference was not one of those cited by Senator Fulbright as being dominated by extreme right-wing views, and it



would have been awkward for the White House to refuse to send a routine message of greeting. Such messages frequently go to groups, the U.S. Chamber of Commerce, for example, whose political views do not coincide with the Administration's. It is less clear why HEW should have let its name be used to give an aura of official sponsorship to the conference. A more serious problem, though, is the connection of these organizations with elements in the Defense Department, since it is not entirely inconceivable that officers indoctrinated by the Forward Strategists could arrange the triggering of a preventive war whether the civilian political leaders want it or not.

The Administration is faced with delicate and interesting problems in dealing with this whole situation, some of which will be discussed in this space next week.—H.M.

### A Lack of Enthusiasm in Detroit

No industry—least of all the much-berated American automobile industry—likes to concede either that its product may be less than wholly beneficial to public well-being or that it is a suitable object for federal regulation.

Perhaps this explains the auto makers' curious reaction to suggestions that they take an inexpensive, and apparently effective, step toward reducing the contaminants that are deposited into the air by the conventional gasoline engine.

The industry is going to take the step, says a spokesman for the Automobile Manufacturers Association, but only, says the spokesman, because it is easier to do that than to convince the public that the industry is the victim of some well-intentioned but misinformed do-gooders.

Under pressure from a variety of sources, and an outright 1964 deadline from the Department of Health, Education, and Welfare, the manufacturers are on the way to adopting as standard equipment so-called blow-by devices. These are designed to reduce substantially the quantity of unburned gasoline that slips past the piston rings and into the air through the crankcase breather. The devices vary, but, according to the industry, they cost \$4 to \$6.50, installed, in California, where the industry, under pressure from the legislature, has "voluntarily" made them standard equipment over the past year.

Basically, the devices consist of a

tube that routes crankcase fumes back to the engine, where they are burned.

Unaffected by this device is the exhaust pipe, which emits an estimated 70 percent of automotive fumes. Its control is a far more complex, and far costlier, task.

Governmental attention, at present, is directed to the crankcase fumes, for these are now considered to be manageable. The Department of Health, Education, and Welfare says it will not "blackjack" the industry into prompt efforts at control, and Secretary Ribicoff was willing to set his deadline for the 1964 models. At the same time, Senator Neuberger said that if the deadline is not met, she will introduce legislation to make blow-by control mandatory. HEW has conveniently drafted a bill for her, and it is on hand in her files as a warning to industry.

Without any apparent enthusiasm, the manufacturers concede that they are going ahead with plans to test and produce the device in time for the deadline, although the federal government is satisfied with currently available devices and requires them as standard equipment on all cars purchased for its civilian agencies.

For a group that has never hesitated in the past to tout production changes, real or imaginary, the auto industry has been strangely silent in public about the blow-by device, which, at extremely moderate cost, holds out the promise of considerable public benefit.

The industry has cited difficulties with one model that incorporated a blow-by device, but the California Motor Vehicle Pollution Control Board has been told that in Los Angeles blow-by devices have been found trouble-free after 2.5 million miles of testing.

The auto industry insists, however, that "conditions are unique" in California, and that the device will be of little benefit elsewhere. In addition, at even \$4 per car, the industry points out, the device will boost the retail price of a year's production by \$25 million.

In any event, this modestly priced device, beneficial or not, has stirred the industry out of proportion to its cost or the mechanical problems involved.

In view of various proposals for federal action to require manufacturers to put more emphasis on public well-being in their designs—for example, seat belts as standard equipment—it is not surprising that anything resembling an opening wedge would be coolly received.

## Announcements

One of the objectives of the Soviet Union's 1958-1965 Seven Year Plan for the improvement of public health is a 350-percent increase in the production of drugs, medical supplies, and equipment for medical research. According to the Soviet report *New Technology in Medicine* (1960), now available in English, the U.S.S.R. has two institutes organized solely to coordinate these efforts, plus special bureaus to develop and modernize medical equipment. The report, translated by the U.S. Department of Commerce, discusses new developments in diagnostic procedures, modern therapeutic apparatus, "mechanized" surgery, prostheses, and new medical materials. (Office of Technical Services, USDC, Washington 25, D.C. \$1.25)

The following publications on the nation's human resources have been released by the U.S. Department of Health, Education, and Welfare:

*Health, Education, and Welfare Trends*. Presents annual data on developments and needs for the several past decades and projections to the 1970's (\$1).

*Handbook on Programs of the U.S. Department of Health, Education, and Welfare*. This includes program analyses and 5-year summaries of statistics showing the program dimensions and trends (\$1.75).

*Grants-in-Aid and Other Financial Assistance Programs*. Contains statistical and other information on all such programs administered by the department (\$1.50).

A group of Russian scientists have arrived in England to discuss solid-state physics research with their British counterparts. This is the first in a series of exchange visits between the two countries, being arranged under an agreement signed last May, for collaboration on peaceful uses of atomic energy.

A new "literature-searching" service in science and technology, initiated by the U.S. Department of Commerce, provides a subscriber with (i) a bibliography of current material in his field at designated intervals, or (ii) a bibliography of all pertinent material available at the time of request. The bibliographies are compiled from government research reports, unclassified and declassified AEC reports, technical trans-

lations and government-owned patents, and material from the science and technology section of the Library of Congress. The fee for the service is \$8 per hour. (USDC, Office of Technical Services, Washington 25, D.C.)

## Meeting Notes

An international symposium on **plant tissue and organ culture** will be held at the University of Delhi from 22 to 29 December. The symposium is jointly sponsored by the university and the UNESCO South Asia Science Cooperation Office in New Delhi. (P. Maheshwari, University of Delhi, Delhi, India)

An international conference on the **use of radioisotopes in animal biology and the medical sciences** will be held in Mexico City from 21 November to 1 December. (Conference Secretariat, International Atomic Energy Agency, Kaerntnerring 11, Vienna, Austria)

The first symposium on **radioecology**, sponsored by the Atomic Energy Commission, Colorado State University, and the American Institute of Biological Sciences, will be held at the university from 10 to 15 September. The conference will cover fallout, disposal of atomic wastes, residual radioactivity near weapon-testing sites, and peaceful uses of atomic energy. (Lewis B. Thomas, Information Service, Colorado State University, Fort Collins, Colorado)

An interdisciplinary symposium on the "expanding goals of **genetics in psychiatry** (1936-1961)" will be held in New York on 27 and 28 October, in conjunction with the sixth annual meeting of the Eastern Psychiatric Research Association. The program will cover functions and future objectives of a genetics department in the psychiatric area; past and present research activities in psychiatric and behavioral genetics; and recent advances in basic genetics. (Franz J. Kallmann, New York State Psychiatric Institute, 722 W. 168th St., New York 32)

A conference on mathematical models in the social and behavioral sciences will be held 2-5 Nov. at Cambria, Calif., under the auspices of the Western Management Science Institute, UCLA. Technical papers in psychology, sociology, business administration, political

science, economics, mathematics, and biology will be presented and discussed. Contributions should report empirical findings and indicate possible approaches to the empirical testing of the model or theory. Topics in interpersonal and group behavior, and personality, theory, especially in its implications for social interaction, are of particular interest. (Fred Massarik, co-chairman, Mathematical Models Conference, Graduate School of Business Administration, University of California, Los Angeles 24)

The first inter-American conference on **congenital defects**, with participants from the U.S., Canada, and Mexico, will be held 22-24 January 1962 at the Statler Hotel, Los Angeles. (Stanley E. Henwood, International Medical Congress, 120 Broadway, Room 3013, New York 5)

A 1-day symposium on the use of **high power accelerators in space science, research, and industry** will be held on 13 October in New York. The symposium is the first in a series to be sponsored by Radiation Dynamics, Inc., a manufacturer of accelerators. (Radiation Dynamics, Inc., Westbury, N.Y.)

An international seminar on **instructional television** will be held at Purdue University from 8 to 18 October. Plenary sessions on 8, 9, 10, and 18 October will be open to the public. From 11 to 17 October there will be a series of work sessions on developments in educational television in the various countries where television has been used as a teaching medium. (U.S. National Commission for UNESCO, Department of State, Washington 25, D.C.)

## Courses

A 3-year **graduate training program in cardiology** has been designed for physicians interested in an academic career in medicine. It combines courses at the Massachusetts Institute of Technology with experience in laboratory and clinical research, and in clinical cardiology at the New England Center Hospital. (M. S. Raben, New England Center Hospital, 171 Harrison Ave., Boston 11)

A course in **urologic radiology** will be given at the University of Minnesota's Center for Continuation Study, 6-10 November. (W. Albert Sullivan,

Jr., University of Minnesota Medical School, 1342 Mayo Memorial, Minneapolis 14)

A new **radiotherapy training program** has been inaugurated at the Stanford School of Medicine. The program, correlated with a newly established radiotherapy research ward and radiobiology research program, takes 3 years; an optional fourth year may be taken at another institution. Prerequisites include one year's internship. Additional experience, particularly in surgery or pathology, is desirable. (Henry S. Kaplan, Department of Radiology, Stanford Medical Center, 300 Pasteur Drive, Palo Alto, Calif.)

## Scientists in the News

**James A. Van Allen**, chairman of the department of physics and astronomy at the State University of Iowa, will receive the Franklin Institute's Elliott Cresson medal for his discovery of the radiation belts around the earth which bear his name.

Two recent Fulbright grants:

**Robert E. Holland** will do research at the Institute of Physics at the University of Helsinki, Finland.

**Robert Vandenbosch** will do research at the Institute for Theoretical Physics, Copenhagen, Denmark.

Both men are staff members of the Argonne National Laboratory.

Recent staff appointments at the National Aeronautics and Space Administration:

**Thomas F. Dixon**, chemical engineer and vice-president for research and engineering of North American Aviation's Rocketdyne Division, has been named director of NASA's Office of Launch Vehicle Programs.

**Frank B. Voris**, director of the Aviation Medicine Technical Division in the Navy's Bureau of Medicine and Surgery, has been named assistant director for aerospace medicine in NASA's Office of Life Science Programs.

**Morris Lieberman**, **Charles C. Craft**, and **James E. Baker**, plant physiologists with the U.S. Department of Agriculture, have been assigned to head the Department's new laboratory for basic research on postharvest physiology of fruits and vegetables. The laboratory is located at the Plant Industry Station, Beltsville, Md.

**Austin Henschel**, of the Quartermaster Research and Engineering Command, Natick, Mass., has been appointed chief of the physiology section in the Public Health Service's Occupational Health Research and Training Facility, Cincinnati, Ohio.

**Harry G. Romig**, senior scientist and staff member of Operations Research, Inc., has been named corporate director of quality engineering of Leach Corporation, Los Angeles, Calif.

Recent staff appointments in the University of Delaware's physics department:

**Ferd E. Williams**, of the General Electric Research Laboratory, will become professor and chairman of the department. He succeeds **Frederick W. Van Namee, Jr.**, who will continue as professor of physics.

**John W. Preiss**, of the National Institutes of Health, will become associate professor.

**Vincent J. Keenan**, of the Institute for Defense Analyses, Washington, D.C., has been elected president of the Philadelphia College of Pharmacy and Science. He will serve the unexpired term of **Ivor Griffith**, who died in May.

Recent appointments to the faculty of the Stanford School of Engineering have been announced:

**Thomas Kane**, associate professor at the University of Pennsylvania's Towne School of Mechanical and Civil Engineering, has been named professor of engineering mechanics and mechanical engineering.

**Rolf Eliassen**, acting head of Massachusetts Institute of Technology's department of civil and sanitary engineering, will become professor of civil engineering, a new position established through a grant from the U.S. Public Health Service.

**Gardner Middlebrook**, director of research and laboratories at the National Jewish Hospital, Denver, is in Argentina as a research consultant and postgraduate lecturer on bacteriology and immunology, under the auspices of the Faculty of Medical Sciences, Buenos Aires University.

**Frederick B. Llewellyn**, assistant to the president of Bell Telephone Laboratories, has been appointed research physicist at the University of Michigan Institute of Science and Technology.

**Meredith P. Crawford**, director of George Washington University's Human Resources Research Office, has received the Army's Distinguished Civilian Service medal.

**Paul A. Clifford**, analytical chemist and consulting editor of the Association of Official Agricultural Chemists, will receive the association's 1961 Harvey W. Wiley award.

**L. Jackson Laslett**, currently with the Office of Naval Research in London, has been named head of the U.S. Atomic Energy Commission's high-energy physics program in the AEC's Division of Research. He has been on sabbatical leave from Iowa State University, where he was professor of physics and senior physicist at the university's Ames Laboratory.

**J. F. Snell**, former head of the radio-biochemical department of Charles Pfizer and Company, Maywood, N.J., has been appointed professor of agricultural biochemistry at Ohio State University.

**J. S. McKenzie Pollock**, World Health Organization representative to the United Nations Relief Works Agency, Beirut, has received a 1-year appointment as associate clinical professor of international health at Harvard.

**Roy L. Swank**, professor and head of the University of Oregon's neurology division, is on sabbatical leave at the Biochemical Institute, University of Cologne.

**Arthur E. Duwe**, associate professor in the department of zoology, Lamar State College of Technology, has been appointed associate professor of natural sciences at Pace College.

**Thornton C. Fry**, mathematician and former vice president for research and engineering of the Sperry-Rand Corporation, has been named consultant to the director of the National Center for Atmospheric Research, Boulder, Colorado.

**Clifford C. Furnas**, chancellor of the University of Buffalo and former Assistant Secretary of Defense, and **Fredrick Seitz**, head of the University of Illinois' physics department, have been named chairman and vice-chairman, respectively, of the Defense Science Board.

**Chandler McC. Brooks**, chairman of the physiology department at the State University of New York Downstate Medical Center, will spend a 1-year sabbatical leave in Japan as visiting professor at the medical schools of the universities of Tokyo and Kobe.

**Ladis D. Kovach**, professor and acting head of the department of mathematics and physics at Pepperdine College, has received a part-time appointment as visiting professor at the University of California, Los Angeles, in the department of engineering.

## Recent Deaths

**Stuart J. Bates**, 74; emeritus professor of chemistry at California Institute of Technology; 28 July.

**William Blaschak**; research histologist in the Veterans Administration Hospital's research laboratory, Pittsburgh, Pa.; 29 July.

**Robert Dax**, 73; physician, and a founder of the American Hospital at Neuilly, France; 8 Aug.

**H. T. Güssow**, 81; Dominion Botanist of Canada for 33 years; associate director of science service, Department of Agriculture, Ottawa; 15 June.

**William A. MacDonald**, 65; electronics engineer and chairman of the board of the Hazeltine Corporation, New York, N.Y.; 11 Aug.

**Agenor Couto de Magalhães**, 66; biologist and chief of the Brazilian government's Fish and Wildlife Service Section, Directorate of Animal Industry, from 1930 until his retirement in 1960; 5 July.

**Simon Rothenberg**, 78; psychoanalyst who studied with Freud; former clinical professor of neurology at Long Island Medical College and chief of the Brooklyn Jewish Hospital's neurological clinic; 10 Aug.

**Harold W. Streeter**, 77; sanitary engineer and consultant with the U.S. Public Health Service; former director of the Robert A. Taft Sanitary Engineering Center; 6 Aug.

**W. P. Van Wagenen**, 64; chief of neurosurgical service at the University of Rochester School of Medicine until his retirement in 1953; 6 Aug.

**Clifford W. Wells**, 76; former physician with the Rockefeller Foundation who specialized in tuberculosis control abroad for 20 years; head of the New Hampshire Health Department's division of communicable diseases until 1958; 5 Aug.



## The "Two Cultures" within Biology

The Virus Laboratory makes a notable effort to contact biologists and laymen outside the walls.

Garrett Hardin

The explosive growth of molecular biology during the last decade has been greeted with cries of joy by most professional biologists, whether or not they are personally engaged in this type of research. Though molecular biology is clearly in its infancy, it is already well enough developed to make it apparent that the intimate and necessary interrelations of structure and function are going to be revealed with a profundity scarcely dreamed of a generation ago. Molecular biology is unquestionably a genuine frontier—not a mere fad—and it deserves generous support.

But every advance creates problems, and this one is no exception. Those who take an interest in the sociology of science have noted, with concern, the widening gap between the biology of research laboratories and the biology of educational institutions. Of course, such a gap exists to some extent in the physical sciences as well, but it is not as threatening. The inhabitant of the physical research laboratory has a historical connection with educational chemistry or physics, for he was trained in university departments of physical science. But the inhabitant of a biological research laboratory often has quite a different sort of relation to the academic world. Examine the roster of any notable laboratory devoted to the study of cancer, viruses, biochemical genetics, or the other branches of molecular biology, and you will discover not only that many, and in some cases the vast majority, of the principals do not have a connection with academic biology but that they have never had one. They may have been trained as physicists, chemists, mathematicians, or astronomers; few of them have ever had even one course in biology.

Is this bad? Considering the mag-

nificent advances in biology which have recently been made by such men, it would be ridiculous to say that their training is inadequate. The danger is rather of another sort, a danger that academic biology, if too long cut off from the most vigorous growing points of biological research, may atrophy. If we move toward a system in which almost all of the workers in certain fields of biology neither receive nor give courses in biology, the result will surely be bad for the academic part of biology (however it may be for the research branch). Within the framework of biological science, we seem in danger of developing "two cultures" reminiscent of the larger ones to which Snow so persuasively called our attention in *Two Cultures and the Scientific Revolution* (Cambridge University Press, 1959). A recognition of this danger is implicit in Commoner's recent paper "In defense of biology" [*Science* 133, 1745 (1961)].

What is to be done? Possibly planning within universities can put a brake on the speciation process by requiring physical scientists to take at least one biology course (this course must, of course, be respectably difficult in their eyes). There is also a need to get some of the laboratory workers out of their labs now and then and onto figurative soapboxes to tell the rest of the world what they have been doing.

### One Lab's Soapbox

Something of this sort happened recently at the Virus Laboratory of the University of California at Berkeley. The result has now been published in two forms, first as a book, *Viruses and the Nature of Life* (Dutton, New York,

1961. 224 pp. \$4.95), and second as a series of eight half-hour films with the general title *Virus* [individual film titles are: (i) *Between the Living and the Non-Living*; (ii) *Giant Molecules*; (iii) *The Stuff of Life*; (iv) *Viral Genes*; (v) *How a Virus Kills*; (vi) *Threads of Life*; (vii) *Killers and Carcinogens*; and (viii) *Cancer*]. The films are marketed by the Audio-Visual Center, Indiana University, Bloomington (rental per film, \$5.25; purchase, \$125 per film). Authorship of both book and films is given as Wendell M. Stanley and Evans G. Valens, with spot credits given to H. L. Fraenkel-Conrat, C. A. Knight, A. B. Pardee, H. Rubin, G. S. Stent, and R. C. Williams. Both book and films are by-products of a series of educational television programs first presented by station KQED in San Francisco.

There are many problems connected with getting busy research men to abandon their work for awhile to do their bit for education (understood in the widest sense). Money is by no means the only problem. At least equally important is the assurance that what they do will have a reasonable chance of being effective. The present effort implicitly offers a formula for maximizing the probable effectiveness: a "package deal," in which a single large effort produces messages over several different channels, namely TV shows, educational movies, and books. The review that follows is concerned not only with the content of these messages but also with my estimate of the present and future success of such package deals.

One of the educational assets of a large enterprise like this is that the producers can "think big." Splendid models of viruses were produced at a magnification of 65 million. On the cinema set these dwarf the human speakers, which is rather a good way to give a feeling of being at an intracellular level. An understanding of size is created by a carefully graded series of photographs ranging from the whole tobacco leaf, through hair cell and macrocrystal of tobacco mosaic virus (TMV) down to TMV particles seen under the electron microscope. The operations involved in isolating viruses are pictured and described with great clarity and economy by Robley Williams. Other workers discuss viruses as organisms, how viruses reproduce and undergo mutation, how genetic information is coded, and how

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viruses affect metabolism and cause disease. Stanley gives a restrained discussion of the possible relationship of viruses to cancers.

### Pros and Cons of Success

How successful is this venture into multiple publication? Speaking generally, I think the result is good and sets an example that could well be followed by other laboratories, to the benefit of both science and the public. The stature of the participants vouchsafes the accuracy of the presentations; interest and clarity are high throughout. Without tendering more well-earned praise, let me now offer a few adverse criticisms, on the assumption that the example here set will be followed by other laboratories, which will not want to make the same mistakes.

The principal shortcoming of the book is what one would expect of a work written by many busy men: looseness and repetition. The word *plaque*, for instance, is defined on page 80 and again on page 115. On page 124 we are informed that "more than 200 previously unknown viruses causing disease in man have been discovered since 1955 . . ." only to be told the same thing again 18 pages later. The organization and writing is somehow unliterary (or unbooklike, at least) and reveals its "stagey" origin. It reads in places almost like a TV script, which some readers will no doubt find annoying. On the other hand, this same origin is no doubt responsible for the unusually close and beautiful integration of text and illustrations, which can stand as a model of excellence. In sum, the shortcomings are minor, and the book can be warmly recommended to intelligent laymen, to high school students, and to both students and faculty, at the college level, who are not in close contact with research in molecular biology.

Evaluating the films is a bit more difficult, because of my uncertainty about their intended use. For TV, one should highly recommend them as a great improvement on the bulk of television fare. Even so, the films have their weak points. The exhibition of the giant models is repeated in more than half the films, and we are told repeatedly that, on this scale, the whole TMV molecule would be six stories high. Once, or possibly twice, would surely be enough. Some anemic chamber music is used as a background

theme for the beginning and the end of all eight films. I found this music positively allergenic, and  $2 \times 8 = 16$ . Some of the art work is quite poor. That the dog in the first film appears to have been drawn by James Thurber at the age of four may not matter much, because everyone knows what a dog looks like; but the diatom is another matter. In the fifth film the animations of the assimilation of food by a cell will surely lead to misconceptions. Admittedly, good animations are expensive; but they should be done well or not at all.

The films were made initially for TV. Are they satisfactory for the college classroom? Yes; but they need further editing. Such statements as "Last week you saw . . ." are out of place here. And the opening few minutes of all but the first film should be deleted to minimize repetition. There is great variation in the stage competence of the speakers, but this is not entirely a shortcoming. Some awkwardness conveys an air of authenticity. The individuality of attire (coats, lab coats, and shirt sleeves) also says, "These are the men who did the work, not actors." That's good.

Probably not many institutions will care to use all eight films, but two at least should see wide use: No. 2, which shows the basic physical procedures involved in virus study, and No. 8 (on cancer), which ends dramatically with a listing of unanswered questions.

Stanley and his group at the Virus Laboratory deserve praise for so ably making their findings available to other scientists and to the general public. Let us hope that other laboratories follow their lead—and that they do even better.

### Garbled Information

**Human Heredity.** Jean Rostand. Translated by Wade Baskin. Philosophical Library, New York, 1961. 139 pp. \$4.75.

For a small book, this one packs a powerful lot of misinformation and misconception. Responsibility must rest mainly with the author, but to some extent it also rests with the translator, Wade Baskin of Southwestern State College, and with the publisher, the Philosophical Library, whose bad judgment it was to produce an English edition. The book appeared as *L'Héré-*

*dité humaine* in Paris in 1952. Between 1952 and 1961 the field of human genetics advanced perhaps as much as during all the period prior to 1952. Some of the misinformation arises from failure of the translation to take account of the advances of the last decade, but other misinformation and most of the misconception had no excuse for their existence even in the original book in 1952. It is interesting to contrast this with Penrose's beautiful little *Outline of Human Genetics* (1959). Rostand's book falls short of its avowed objective: "to introduce the greatest number of people into the sovereign dignity of knowledge." Penrose's fulfills this purpose quite satisfactorily.

Beginning on page 14 where it is stated (and it is later repeated many times) that the chromosome number of man is 48, misinformation piles up in great mounds. Inadequate compensation is provided by the translator in fine print in the appendix: "It has recently been established that there are only forty-six chromosomes." Several times serious reservations are raised, and discussed at some length, concerning the existence of the Y chromosome in man. The reader is told that the founder of modern genetics was Johann Mendel—correct since the full name was Johann Gregor Mendel, but certainly unusual.

Men with many daughters will be intuitively suspicious of the view repeated on page 126 that "there is probably a correlation between the tendency to produce boys and the virility of the father." On page 132 we read "out of ten stillborn children, three are victims of maternal syphilis"—a statement which simply is not true and probably never has been, at least not in recent decades. Historical and genetic information alike are garbled on page 78 where the now famous story of Queen Victoria's transmitting hemophilia is related. "Victoria received it from her mother, who had received it from her mother." Haldane has investigated the matter most closely and thinks there is no evidence that the gene existed in the lineage before Victoria and that she was a carrier by virtue of new mutation. "Victoria's husband, Prince Albert of Saxe-Coburg-Gotha belonged to a progeny of carriers, though he himself was probably illegitimate." Irrelevant and probably untrue!

The grossest misconception conveyed by this and unfortunately by several other popular and semipopular

presentations of human genetics, some of them written much more recently, is that the inheritance of eye color, hair color, form, and any number of other normal and disease traits is a simple matter of Mendelism. For example, long lists are provided with these traits arranged down the pages in columns according to whether they are dominant or recessive. The inheritance of none of the traits, particularly the "normal" ones, is all that simple. In connection with rare hereditary disease traits, such treatment misses an important concept of medical genetics, namely, the heterogeneity of entities which phenotypically appear to be homogeneous.

The author, a biologist, is the son of Edmond Rostand (1869-1918), creator of *Cyrano de Bergerac*, and the brother of Maurice Rostand, also a dramatist.

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## La Vie

**Encyclopédie Française.** vol. 4, pt. 1 and pt. 2, *La Vie*. Fondement, maintien, reproduction. Pierre-P. Grassé, Ed. Société Nouvelle de l'Encyclopédie Française. Larousse, Paris, 1960. x + 710 pp. Illus. + plates.

Seventy of France's distinguished scientists participated in the writing of this book. They have avoided an encyclopedic collection of fragments and have produced an organized, logical account of biology.

*La Vie* is composed of nine sections, each with a number of chapters (the number is indicated in parentheses). Origin and Place of Life (2) discusses theories of the origin of life, physical functions of living matter, and geobiochemical cycles of carbon, nitrogen, and other elements. Physical Structure and Chemical Composition (4) considers, among other topics, colloidal state, water absorption, birefringence, macromolecules in protoplasm, energy transfer, and the chief chemical constituents of living things. Organization of Living Beings (7) deals concisely with the cell concept, bacterial morphology and sexuality, viruses, cytology of the animal cell, the multicellular state and cellular differentiation, and cytology of the plant cell. Cellular Activities (7) is de-

voted to several subjects of general physiology such as ameboid and muscular movement, cell permeability, water and ion exchange in plant cells, enzyme action, processes of synthesis and degradation, and the relation of physicochemical laws to cell activities. Maintenance in Animals (11) and Physiological Equilibrium (6) review, essentially at the organismal level, the comparative physiology and biochemistry of the principal physiological processes and such other topics as production of light and electricity, immune reactions, wound healing, animal grafts, and tissue culture. Behavior (11) deals with sensory information, the nervous system, the nerve impulse, simple reflex and higher nervous activity, sleep and rhythmic activities, tropisms and reflexes, instinct, intelligence, and social phenomena. Maintenance in Plants (9) is a section on plant physiology with consideration of structural and functional diversity, energy sources, plant anatomy and organogeny, synthetic processes, mineral metabolism, physiological regulation, growth and morphogenesis, movements and tropisms, and reactions to environmental factors. The book ends with the section Transmission of Life (6) in which are discussed sexual and asexual reproduction, animal ontogeny, growth, senescence and death, plant reproduction, and heredity.

Many line drawings illustrate the text. The 32 plates contain 90 figures; 35 of these are photographs, predominantly of protozoan, invertebrate, and plant forms, taken through the electron microscope.

One appendix consists of bibliographic references grouped by chapter headings; another contains brief academic *vitae* of the contributors. There are 30 pages of subject index. Both appendixes and the subject index are duplicated in each volume.

My initial apprehension, caused by a dust jacket claim that the use of too technical terms had been banned, was allayed by reading a few selected chapters. The book is no mere popularization of biological principles. *La Vie* aims at an explanation of laws regulating living organisms; its approach is largely that of molecular biology. In a foreword Gaston Berger phrases this astutely, if perhaps idealistically: "The chemist, studying the reactions that operate in an organism, devotes himself to following molecules, atoms and particles through the various systems in which they participate. The biologist,

studying the same processes, endeavors to discover how organization results from the elements, function from the reactions."

Striking changes in the introductory biology courses of many colleges will soon be necessary as a result of the national efforts to improve biology teaching in secondary schools. A judiciously edited translation of *La Vie* could be a model in planning and organizing an undergraduate course for students who come with the new secondary school preparation in biology and chemistry.

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## Ineffective Committees

**Biological Education in American Secondary Schools, 1890-1960.** Biological Sciences Curriculum Study Bulletin No. 1. Paul DeHart Hurd. American Institute of Biological Sciences, Washington, D.C., 1961. x + 263 pp. \$4.75.

In this book Hurd reviews biology teaching in American secondary schools from 1890 to 1960. The book consists of two parts: reports of various curriculum committees and reports of research studies.

Part 1 consists of recommendations from 84 biology curriculum committees plus the author's explanatory comments. The 70-year period is divided into the seven decades, and a chapter is devoted to each.

Presumably the reports of the various committees were intended to improve biology teaching. However, little evidence is presented to show that they have had much effect. Hurd writes: "There is no real way to judge the extent to which the biology curriculum committees . . . were effective in bringing about change in either the content or conduct of biology courses. It is apparent that the ideas for improvement of biology teaching being discussed today are quite similar to many of those suggested before the turn of the century."

Why, then, was so much of the book devoted to useless reports? Perhaps the author thought a demonstration of past ineffectiveness would secure the efforts of future committees, for he also writes: "An analysis of the factors involved in getting curriculum reforms into the

educational stream and to the point where they have an impact on the education of the student is sorely needed." Following this statement he lists seven possible reasons why recommended curriculum changes were ineffective.

Part 2 includes six chapters that review the literature of research on biology teaching. The areas reviewed are books on the teaching of secondary school biology, objectives of high school biology, criteria for the selection of course content, biology textbooks, learning of biology, and instructional resources. One chapter is devoted to unresolved problems in biological education and another to problems and issues in biology teaching.

The value of the book is due largely to part 2, which presents under one cover a vast amount of otherwise scattered information. The author's analysis of the ills and problems of secondary school biology is particularly good.

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## Probability

### **The Algebra of Probable Inference.**

Richard T. Cox. Johns Hopkins Press, Baltimore, Md., 1961. x + 114 pp. \$5.

The answer to the common question as to what probability "really is" is the demonstration that any quantity measuring the chance of an event and having the properties we would expect must be the probability we know. These assumed properties may be the axioms of measure theory but, for the specific case of probability, simpler and more intuitive assumptions can be used.

In this book, Richard Cox begins by deriving the elementary laws of probability from nothing but the Boolean algebra of logic (which he develops convincingly on the spot) and the following two eminently reasonable axioms:

1) The probability of an inference on given evidence determines the probability of its contradictory on the same evidence;

2) The probability on given evidence that both of two inferences are true is determined by their separate probabilities, one on the given evidence, the other on this evidence with

the additional assumption that the first inference is true.

Care is taken to make clear what follows willy-nilly from the axioms and what is arbitrary. The author acknowledges his indebtedness to Keynes's *A Treatise on Probability*, and he has sensibly retained some of the good features of that work—for example, the insistence that a proposition can have a probability only in relation to a given hypothesis.

In the remaining two-thirds of the book, two other concepts, whose "real meaning" is often questioned, are also developed from simple axioms. These are the concept of the entropy (in the information theory sense) of a system of propositions and the concept of expectation. The book closes with a five-page explanation of inductive argument, which could be recommended anywhere as a text for this much misunderstood basis of the scientific method.

Throughout the book the proofs, starting as they do from first principles, are unavoidably laborious, and this, combined with the pleasant but discursive style of the text, often makes it difficult for the reader to keep track of the over-all course to be sailed. The use of notation which is neither standard nor mnemonically suggestive adds to the difficulty of the reading. Nevertheless, the work is there, and the book might be read with considerable interest, not as a text (for which it was not intended) but as outside reading, by any student or professional who is working in the field of probability, statistics, or information theory and who would appreciate a different approach to the groundwork of his field. The author neither treats mathematics as a bag of tricks nor forgets the applications of the subject.

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## New Books

### General

**Advances in Documentation and Library Science.** vol. 3, part 2, *Information Retrieval and Machine Translation*. Allen Kent, Ed. Interscience, New York, 1961. 698 pp. Illus. \$25.

**Air Bombardment.** The story of its development. Sir Robert Saundby. Harper, New York, 1961. 271 pp. Plates. \$5.

**American Industrial Research Laboratories.** Frederick A. White. Public Affairs Press, Washington, D.C., 1961. 239 pp. \$6.

**Doctors, Patients and Health Insurance.** The organization and financing of medical care. Herman Miles Somers and Anne Ramsay Somers. Brookings Institution, Washington, D.C., 1961. 595 pp. \$7.50.

**The Philosophical Impact of Contemporary Physics.** Milič Čapek. Van Nostrand, Princeton, N.J., 1961. 431 pp. \$7.50.

**Seeds.** The yearbook of agriculture. U.S. Department of Agriculture, Washington, D.C., 1961 (order from Supt. of Documents, GPO, Washington 25). 605 pp. Illus. + plates. \$2.

**Springtime of the Stars.** Georges Beau. Translated from the French by Hector A. Chiselscharpe. Criterion Books, New York, 1961. 149 pp. \$3.95.

**Teaching and Learning in Medical School.** George E. Miller, Ed. Harvard Univ. Press, Cambridge, Mass., 1961. 317 pp. \$5.50.

### Mathematics, Physical Sciences, and Engineering

**Antenna Engineering Handbook.** Henry Jasik, Ed. McGraw-Hill, New York, 1961. 1060 pp. Illus. \$22.

**Basic Concepts in Modern Mathematics.** John E. Hafstrom. Addison-Wesley, Reading, Mass., 1961. 205 pp. Illus. \$5.75.

**Elementary Mathematical Analysis.** A. E. Labarre, Jr. Addison-Wesley, Reading, Mass., 1961. 718 pp. Illus. \$7.75.

**Fuel Element Fabrication.** With special emphasis on cladding materials. Proceedings of a symposium held in Vienna, 10-13 May 1960. Academic Press, London, 1961. Illus. vol. 1, 549 pp., \$14; vol. 2, 396 pp., \$10.

**Geologie Von Bayern.** Adolf Wurm. Gebrüder Borntraeger, Berlin, 1961. 572 pp. Illus. DM. 96.

**An Introduction to the Analysis of Spin-Spin Splitting in High-Resolution Nuclear Magnetic Resonance Spectra.** John D. Roberts. Benjamin, New York, 1961. 122 pp. Illus. \$4.95.

**Introduction to Nuclear Engineering.** Raymond L. Murray. Prentice-Hall, Englewood Cliffs, N.J., ed. 2, 1961. 397 pp. Illus. Trade edition, \$12; text edition, \$9.

**Introduction to the Theory and Applications of Dispersion Relations.** M. L. Goldberger. Wiley, New York, 1960. 671 pp. Illus.

**Meteor Science and Engineering.** D. W. R. McKinley. McGraw-Hill, New York, 1961. 318 pp. Illus. \$12.50.

**Progress in Very High Pressure Research.** Proceedings of an international conference held 13-14 June 1960. F. P. Bundy, W. R. Hibbard, Jr., and H. M. Strong, Eds. Wiley, New York, 1961. 333 pp. Illus. + plates. \$12.

**The Quantum Mechanics of Many-Body Systems.** D. J. Thouless. Academic Press, New York, 1961. 184 pp. Illus. \$5.50.

**Radioisotope Applications Engineering.** Jerome Kohn, René D. Zentner, and Herbert R. Lukens. Van Nostrand, Princeton, N.J., 1961. 576 pp. Illus. \$16.50.

**Satellite Environment Handbook.** Francis S. Johnson, Ed. Stanford Univ. Press, Stanford, Calif., 1961. 167 pp. Illus. \$5.50.

**Topology.** John G. Hocking and Gail S. Young. Addison-Wesley, Reading, Mass., 1961. 383 pp. Illus. \$8.75.



## Reports

### Natural Tritium Measurements by Ethane Counting

**Abstract.** A method is described for the synthesis of ethane from hydrogen that is at present used for the counting of low-level tritium activity at the La Jolla tritium laboratory. The reaction procedure is simple and involves the mixing of the hydrogen with acetylene over a colloidal palladium catalyst. Counting characteristics of ethane are found to be ideal. With a 1-liter counter filled to three atmospheres of ethane, only a tenfold tritium enrichment is necessary in order to obtain a sensitivity of 0.32 counts per minute per tritium unit.

Hydrocarbon gases are well known for their remarkable counting characteristics. The long flat plateaus, low working voltage, and low sensitivity to impurities make them ideal for gas counting. Acetylene has been used for many years (1) for the counting of low-activity, natural carbon-14.

Hydrogen is the only gas to date that has been used for counting tritium in the gas phase (2). However, the use of hydrogen presents various difficulties. In the Geiger region double and triple pulse formation is very prolific, even with ethylene-argon counting mixtures. Most workers overcome this problem by using external electronic quench circuits. An alternative method previously used by one of us (A.E.B.) is a 1- to 1.5-msec paralysis time in the electronics. The use of hydrogen in the proportional region is also difficult, owing mainly to the steep gas gain versus voltage characteristics, and the ease of formation of negative ions.

**Instructions for preparing reports.** Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to contributors" [Science 125, 16 (1957)].

Use of a hydrocarbon synthesized from water has the following advantages: (i) better counting characteristics; (ii) operation in the proportional region which makes possible background reduction by energy discrimination; (iii) more than two atoms of hydrogen per molecule; (iv) satisfactory operation also at pressures of several atmospheres. Hence, much larger amounts of hydrogen can be put into a counter when converted to a hydrocarbon, without unduly increasing the background. In this way the need for enrichment can be reduced by more than a factor of ten. Consequently, measurements of a considerably greater accuracy can be obtained, because the main error arises from the determination of the enrichment factor, whether it be by electrolysis, distillation, or thermal diffusion, and because the fractional error increases logarithmically with the enrichment.

There are many papers (3) on the reaction



We have tried nickel as a catalyst and the results obtained only add to the general confusion in the literature concerning conditions and end products of this reaction. The main cause of the difficulties encountered is the large temperature coefficient of the reaction and the formation of higher hydrocarbons, including oils and waxes, at higher temperatures. Also, commercially available "palladium on powdered charcoal" catalyst (4) proved to be unsatisfactory for our purpose, because ethane is strongly absorbed on charcoal at room temperature. Satisfactory results, however, were obtained with a palladium catalyst prepared in our laboratory according to the following procedure: Palladium chloride is reduced with formaldehyde in dilute solution with a trace of potassium carbonate added. The colloid is filtered on a Millipore HA filter which is subsequently ashed in a covered quartz crucible. Colloidal palladium is

stable in air at room temperatures, but in the presence of hydrogen changes color from blue to metallic gray as it is transformed to palladium hydride. As only 300 mg of catalyst is used, the loss of hydrogen by this reaction is negligible, but to avoid the possibility of a memory effect, fresh palladium is used for each sample.

The volume of hydrogen is measured in a 12-liter Pyrex flask which also contains the catalyst scattered on the bottom. Half this volume of acetylene is measured in a separate ballast flask and then transferred by freezing into a small trap attached to the reaction flask. The reaction has been tested for volumes of  $\text{H}_2$  up to 6.6 liters and initial total pressures from 20 to 71 cm-Hg. The pressure has no appreciable effect on the reaction rate. In 2 to 4 hours the volume of gas is reduced to the original volume of acetylene. This indicates that the reaction is complete. No further volume reduction occurs, even if the product is left in contact with the catalyst for 48 hours. Analysis by gas chromatography shows that there is no detectable amount of ethylene present in the product. Tank acetylene is used after purification and the hydrogen is generated from the water sample by reduction of water vapor over magnesium at 600°C.

For our counter, with a 3-mil stainless steel center wire and 3 atmospheres of  $\text{C}_2\text{H}_6$ , the operating voltage was 9000 volts. The plateaus for both anticoincidence and meson counts were several thousands volts long, with slopes of 2 percent per 1000 volts. By our use of discriminators, the background was 1.6 count/min for a counter volume of 0.8 liters in the energy range from about 1 to 30 kv. The total background was 5.5 count/min, made up of the following components: pulses produced by neutrons and gamma rays; activity present in the counter material; and alphas partly produced by radon in the tank acetylene. Over the past 6 months we have made control measurements with a tritium standard producing 80 count/min. The reproducibility was better than 0.5 percent. The background of 1.6 count/min in the low-energy channel over the same period did not show any statistically significant fluctuations. The tritium activity is 6.7 disintegrations per minute per liter of water and tritium unit, or  $5.4 \times 10^{-3}$  disintegrations per minute per liter of  $\text{H}_2$  gas at standard temperature and pressure and tritium unit. Hence we observe 0.26



disintegrations per minute with a filling of 3 atmospheres of ethane, and with a sample containing 10 tritium units in our counter, which has a sensitive volume of 0.8 liter. A larger counter (2-liter) is at present being constructed. No effects from isotope separation were observed by using hydrogen of known tritium content. This is in agreement with the fact that the chemical yield of the ethane synthesis is close to 100 percent. Results of tritium measurements currently being carried out at this laboratory will be published elsewhere.

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#### References and Notes

1. H. E. Suss, *Science* **120**, 5 (1954).
2. See for example the summary given by H. v. Buttlar and W. Stahl, *I.A.E.A. Symposium on Detection and Use of Tritium, Paper TTS/4* (Vienna, May 1961).
3. See, for example, G. Egloff, *Reactions of Pure Hydrocarbons* (Reinhold, New York, 1937); R. E. Dodd and P. L. Robinson, *Experimental Inorganic Chemistry* (Elsevier, Amsterdam, 1954).
4. K. Tamaru, *Bull. Chem. Soc. Japan* **23**, 64 (1950) and **24**, 177 (1951).
5. This work is supported by a contract with the Air Force Cambridge Research Center, Geophysical Directorate, Bedford, Mass. Laboratory instrumentation was provided from a grant from the Division of Biology and Medicine, Atomic Energy Commission. One of us (A.E.B.) is on leave from the Department of Scientific and Industrial Research, New Zealand.

6 June 1961

### "Hypersexuality" in Male Cats without Brain Damage

**Abstract.** During 5 years of observation in a cat colony where mating tests are routinely conducted, the spontaneous occurrence of distortions of sexual activity in male cats has been recorded. Many of the behavioral patterns encountered have previously been described only in brain-damaged animals when they have been used as an index of "hypersexuality." Identical behavior occurs in normal males as a simple training effect.

The possible role of the temporal lobe in the normal regulation of sexual activity has remained a question of considerable interest since Kluver and Bucy described striking alterations in the sexual behavior of mature rhesus monkeys in the weeks after bilateral temporal lobectomy.

There is no doubt whatever that sexual manifestations in primates of both sexes increase, both in range and frequency, after such surgical interven-

tions (1, 2). Observations of a similar type have been extended, on rather less secure grounds, to several infraprimate species, and attention has been given in particular to the sexual activity shown by male cats toward (i) anoestrous, non-receptive female cats, (ii) other male cats, (iii) kittens, (iv) inanimate objects such as a child's woolly toy, and (v) alien species such as dogs, chickens, and rabbits (2, 3). Aberrant behavior of this kind has been widely used as a criterion of abnormal hypersexuality. The observation of the occurrence of such patterns of behavior after destruction of, or lesions in, the amygdala and pyriform cortex has implicated these structures, and the temporal lobe generally, in the regulation of the sexual behavior of the male cat (4).

Some of the reports describing the distortions of sexual activity, which result either from altering the hormone balance or from physical interference with the brain, indicate a lack of familiarity with the range of behavior normally shown by the cat and with the shifts from the normal which can be produced by simple manipulation of the environmental situation. I have conducted several thousand mating tests with the cat during the past 5 years and, therefore, my experience may be of interest to others in this field (5).

If a mature male cat is trained to carry out mating tests with receptive females and is "in territory" within its home cage or test pen and is then presented with another mature male, the latter will invariably be mounted. The mounted male in most instances passively tolerates the neck grip and copulatory thrusts of the mounting male. The sequence of mounting does not depend upon the relative sizes of the animals, but upon the influence of territory; the animal in familiar surroundings in its home cage is dominant. If on a subsequent occasion, the mounted male is established in its own territory (where it has previously mated with receptive females), it will then mount the male by which it had previously been mounted. "Tandem" and multiple mounting occur readily in the laboratory when trained animals are used, and the sequence can be changed indiscriminately by changing the order in which animals are presented. Homosexual behavior in the test situation (in the sense that the sexual object is another male), as well as mounting activity between males housed in pairs, is thus a common observation (6). In contrast

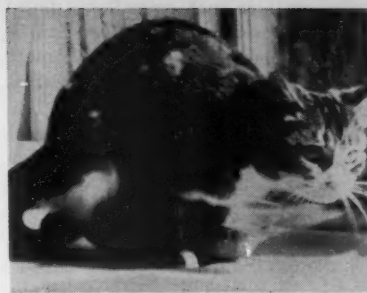


Fig. 1. Mounting activity and ejaculation shown by a normal male cat with a child's toy rabbit (frame from a motion-picture film taken in a private home).

to the foregoing, if two stud males, both of which have frequently mated in a test room and established territory rights there, are liberated in it simultaneously, serious fighting may ensue. It can be seen, then, that totally different behavioral patterns (passive acceptance of mounting or active fighting) can be evoked merely by a rearrangement of the test situation. Inexperienced males can be trained to show intense sexual interest in inanimate objects by alternately presenting a receptive female and some object such as a toy teddy-bear. A male so trained will then mount, secure a neck bite, and attempt copulation with any suitable soft object, including the sleeve and arm of the attendant's coat. Masturbatory activity of various kinds is readily observed in young, isolated males as well as in males housed in pairs, but only when the animals are well adapted to, and familiar with, the environment and not when newly arrived from a dealer.

Of even more interest than the sexual deviations which result from training and conditioning procedures within the laboratory is the occurrence of such phenomena spontaneously in domestic animals. Several reports of sexual activity with inanimate objects have reached me from owners of pet cats. One report, supported by a motion-picture film taken in a private home, describes a mature, intact male (Fig. 1). Although allowed complete freedom and the sire of many litters in the neighborhood, this cat, if left undisturbed, regularly mounted, and attempted copulation with, a child's toy rabbit from which sperm could be recovered. This type of masturbatory activity with an object which appears to stand for the true sexual object may be analogous to fetishism in the human. Careful histological examination of the temporal

lobes of three such animals has failed to reveal the slightest evidence of either Ammon's horn sclerosis or any more obvious pathology. Although aberrant behavior is infrequently reported because of the distaste it arouses in animal owners who, as a consequence, have their pets castrated, it is probably more common than we are accustomed to believe (1). In all this the male cat does not appear to differ from other species of domesticated animals which can be trained to mate with artificial vaginae for sperm collection.

Every variety of abnormal behavior which has been used as a criterion of hypersexuality in male cats has been encountered, with one exception, during the past 5 years of observation of animals without brain damage. The exception is mounting activity toward alien species which I have not observed. Upon this I cannot comment except to observe that such activity may be less specifically related to the sex drive than the visual agnosia which forms part of the temporal lobe syndrome. The patterns of spontaneously occurring abnormal behavior include (i) the tenacious clinging to female partners by males during copulation when attempts at separation are made—so that both animals can be suspended in mid-air, (ii) indiscriminate mounting by males of other males, (iii) tandem and multiple mounting behavior, (iv) neck grips, mounting, and attempts at copulation with kittens of under 900 grams, and (v) masturbatory activity, mounting, and ejaculation upon inanimate objects. This latter phenomenon occurs spontaneously in freely running animals as well as in those subjected to training procedures within the laboratory. Although such phenomena as multiple mounting behavior seem at first to be very bizarre, the expression of identical patterns of behavior in animals which have not been subjected to operative interference suggests the need for caution in the interpretation of results. The observations that are presented here show clearly that many of the manifestations of so-called "hypersexuality" can either occur spontaneously or be produced as a conditioning effect by simple manipulation of the environmental situation.

It would be wrong to infer from the foregoing that the rhinencephalon is not of great importance in the regulation of sexual behavior in the cat and other species; the evidence in the rhesus monkey is overwhelmingly against this. But the spontaneous occurrence of such

behavior in male cats without brain damage implies a need for quantitative studies combined with control procedures aimed at excluding the possible effects of training. Only such measurements will enable the precise role of the temporal lobe in the sexual activity of this species to be evaluated (8).

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4 May 1961

### Spontaneous Occurrence of Chromosome Abnormality in Cats

**Abstract.** A syndrome in male cats analogous to chromatin-positive Klinefelter's syndrome in human males has been demonstrated. The physical characteristics which suggested an abnormality of chromosome number in cats were "calico" or "tortoise-shell" coat colors in a male. Buccal mucosal smears were found to have "female-type" patterns in two out of 12 such male cats screened, and these two were found to have a diploid chromosome number of 39 rather than the normal 38. Testicular biopsy performed on one revealed an abnormal pattern; no gonadal tissue was found in the other cat with an abnormal chromosome number. These findings indicate that the cat, in addition to the mouse, is available for experimental study of chromosome number abnormalities.

Geneticists have been puzzled by the mechanisms involved in the rare male cat with both black and orange colored patches in its coat (1). Under the hypothesis that control of these two coat colors is related to allelic genes on the X sex chromosome (2), both should occur simultaneously only in individuals with two X chromosomes, such as normal females. The reports of males with both black and orange colors have cast doubt upon the hypothesis. However, the observation that a majority of reported "tortoise-shell" or "calico" males are sterile (3) suggests that some unusual mechanism is operating.

The possibility that the male calico

cat might represent a chromosome abnormality comparable to chromatin-positive Klinefelter's syndrome in human males was suggested. Chromatin-positive Klinefelter's syndrome includes a sex-chromatin pattern of "female" rather than "male" type, at least one additional chromosome determined by tissue culture techniques (this is considered to be an X chromosome to give a sex-chromosome complement of XXY), and abnormality of the testicular tubules with failure of spermatogenesis and clinical sterility. If male tortoise-shell and calico cats are feline analogs of human "Klinefelter's" and thereby have two X and one Y chromosomes, the explanation of the presence of both colors in their coats would be simple. The spontaneous presence of such an abnormality has additional interest in that it would permit laboratory study of basic mechanisms involved in an order other than the Rodentia and encourage search for similar anomalies in other species.

Male cats with combinations of three coat colors were examined for the criteria used in the diagnosis of human chromatin-positive Klinefelter's syndrome. Of 12 animals located, only one had typical black and orange patches. The 12 were screened by examining the nuclear chromatin patterns in buccal mucosal cells stained with aceto-orcin. Ten showed the normal male pattern consistent with control male cats tested, but two had the female type, chromatin-positive smears. These two, one being the typically marked calico cat, were examined further.

The one of the two cats with chromatin-positive cells but without the true orange and black spotting had a normal male phallus and a normal scrotum containing descended testes, one of which was removed by excision biopsy. The exposed testis was smaller than normal, measuring 10 by 15 mm, and was firmer than usual. Aceto-orcin squash preparation of fresh biopsy material previously treated with 0.17-percent NaCl solution for 10 min revealed cells in meiotic division, but no spermatids or spermatozoa were seen. This lack of normal spermatogenesis was confirmed by observation of tissue sections stained with hematoxylin and eosin.

The second cat, typically marked, also had a normal male phallus but the scrotum was undeveloped and no testes could be palpated in it or in the inguinal canals. Exploratory laparotomy was done, and no gonadal tissue or internal reproductive system structure could be

identified. The surgery was done by an experienced veterinarian (4), who stated that he had never seen an animal without at least vestigial organs. White blood cells from the two chromatin-positive cats were established in tissue culture (5) by a modification of the method published by Mellman *et al.* (6). Growth was obtained in culture from the first cat, but technical problems limited the number of countable cells to three. These showed 39 chromosomes rather than the normal number of 38 reported by various workers (7) and confirmed by our procedures with blood from normal cats. Better preparations were obtained from the second cat, the typical calico, and the chromosome number in nine cells was also 39. Further work is being done to establish which chromosomes are involved in the abnormality, and we are preparing idiograms for chromosomes in tissue culture from normal and abnormal cats (8). It should be emphasized that this chromosome abnormality would not be limited to the male with calico markings. The rare coat color merely served as a convenient primary screening device.

We feel that this demonstration of a spontaneously occurring chromosome abnormality in which the chromosome number is  $2n + 1$  is an encouragement to seek associations of sex-linked characteristics with such chromosome abnormalities in mammals more suitable than the cat to experimental laboratory study of factors involved in the etiology of such disorders. Russell and his associates (9) demonstrated the occurrence of fertile XO ( $2n - 1$ ) females in a population of laboratory mice. This may or may not be proved etiologically analogous to gonadal dysgenesis in human females, an abnormality in which the sex chromosomes are XO ( $2n - 1$ ). Thus both a decreased and an increased number has now been found in mammals other than humans. The similarity with respect to testicular development between the effect of an extra X chromosome in humans and these cats in which the additional chromosome is presumed to be an X chromosome is also of marked interest in its implication that specific genetic mechanisms may be located on the analogous chromosomes in two differing species. Finally, the utility of the buccal mucosal smear technique in screening individuals for this chromosomal abnormality appears to be valid in cats as well as humans (10).

*Note added in proof:* Since this

report was submitted, L. B. Russell has published a review of the genetics of mammalian sex chromosomes as studied in mice at the Oak Ridge National Laboratory, Oak Ridge, Tenn. [*Science* 133, 1795 (1961)]. She cites the finding of an XXY male mouse, apparently sterile, among 6368 animals observed. The apparent sterility of this mouse extends to three the number of species in which abnormality of gametogenesis is associated with an additional X chromosome in the male.

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26 April 1961

#### Simian Malaria in the Philippines

**Abstract.** The first field study of simian malaria in the Philippines found that malaria occurred in 8.6 percent of the animals tested. Although based on a very limited study, this report suggests that the simian reservoir of malaria is probably of limited significance for the human population in the Philippines.

The first field study of simian malaria in the Philippines has been conducted in view of the recent report of malaria transmission between lower monkeys and humans (1) and because of the possible significance of this finding on current methods for eradicating malaria.

In the western Pacific region, simian malaria has been reported in Taiwan, Borneo, Java, Sumatra, Malaya, and Indochina (2). There are no published

accounts of related studies having been made in the Philippines, but *Plasmodium inui* has been isolated from Philippine monkeys sent to the United States and England (3).

In a preliminary blood survey within the Philippines, 16 positives (8.6 percent) were found among 186 *Macaca irus* (*M. cynomolgus*). From the northern provinces of Cagayan, Nueva Vizcaya, and Bulacan, the sample (24 animals) was negative. From the southern province of Palawan and the island of Mindanao, 16 positives were found in 162 animals.

The infected animals did not appear to be seriously ill. The parasites contained pigment during the trophozoite stage. No enlargement of red cells or Schuffner's stippling was found. The close morphological resemblance to *Plasmodium malariae* suggests the identification of *P. inui*. Halberstadter and Prowazek (4) first described this species in *Macaca irus* and *M. nemestrina* from the island of Borneo, which lies adjacent to the southern boundary of the Philippine archipelago. Since the flora and fauna of the southern islands are similar in many respects to neighboring Borneo, the presence of *Plasmodium inui* in both areas is not an unexpected finding.

For the past several years, the distribution of the Philippine human population has been undergoing a major shift away from the overpopulated coasts and valleys toward newly opened public lands which characteristically lie in hilly uplands bordering forested mountain ranges. Many variables contribute to the high potential for the transmission of malaria along these population frontiers, not the least of which are the many open, sunlit upland streams that constitute a highly favorable breeding habitat for the common Philippine vector, *Anopheles minimus flavirostris*.

It is an associated factor that monkeys are present in large numbers in the forests which lie adjacent to the advancing edge of new settlements. As a general pattern, it is often necessary for the new settler to spend some time within the forest in order to clear and burn his land before he can plant the usual upland crops of rice or corn. Careful assessment of the many epidemiological variables which apply at this geographical location indicates that the human malaria reservoir accounts for the source of all infections which have been investigated up to the present time. While the present report is based



on a very limited study, it does suggest that the simian reservoir is probably of limited significance in the Philippines for the following reasons: (i) *Plasmodium malariae*, which bears the closest resemblance to *P. inui*, was identified in only 26 out of a total of 41,945 positive human blood smears between 1 July 1959 and 30 June 1960. (ii) In frontier settlements, the species of malaria are divided almost equally between *P. falciparum* and *P. vivax*, which are both morphologically dissimilar to *P. inui*. (iii) In the northern Philippines (Luzon), the pattern of malaria parallels the pattern in the southern islands without evidence, so far, that simian malaria is present.

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7 July 1961

### Effect of Actinomycin D on Cellular Nucleic Acid Synthesis and Virus Production

**Abstract.** Actinomycin D inhibits the synthesis of ribonucleic acid in L cells and the yield of vaccinia virus containing deoxyribonucleic acid, but it does not inhibit cellular deoxyribonucleic acid synthesis or the multiplication of Mengo virus containing ribonucleic acid. These observations serve to distinguish the replication of viral ribonucleic from ribonucleic acid synthesis which is controlled by viral or cellular deoxyribonucleic acid.

Actinomycin D is a bright red antibiotic containing two peptides, which was first reported by Vining and Waksman (1). It possesses strong antibacterial activity against gram-positive organisms (2) and, on a weight basis, is the most potent chemotherapeutic antitumor agent known (3). It has been reported to be antimutagenic (4).

Mammalian cells grown in the pres-

ence of actinomycin D lose their nucleoli and much of their histochemically demonstrable ribonucleic acid (RNA) (5, 6). In the present study we report that actinomycin selectively and irreversibly suppresses mammalian cellular RNA biosynthesis, at least up to 48 hours after exposure—the period during which affected cells have been observed.

Strain 929 L-cells monolayers were maintained and propagated as previously described (6). In addition, spinner cultures (7) were employed. Cell monolayers, seeded on cover slips and exposed to suitable radioactive nucleic acid precursors, were examined autoradiographically by the method of Doniach and Pelc (8).

When normal L cells are incubated with  $H^3$ -cytidine (0.5  $\mu$ Ci, 0.4  $\mu$ g/ml, 3 to 6 hours) and inspected after radioautography, a portion of the radioactivity incorporated into acid-insoluble material may be solubilized by deoxyribonuclease. The remainder can be rendered acid-soluble by digestion with ribonuclease.

After exposure to actinomycin D (1.0  $\mu$ g/ml for 8 hours) and subsequent incubation for 16 hours, L cells continue to incorporate  $H^3$ -cytidine into acid-insoluble material. In this case, however, none of the incorporated radioactivity becomes acid-soluble after ribonuclease treatment; all of it is solubilized by deoxyribonuclease. We conclude that cellular RNA synthesis, but not DNA synthesis, has been completely arrested by antecedent incubation with actinomycin.

Similar findings are shown in Table 1, in which pairs of spinner cultures are compared with respect to the incorporation of  $H^3$ -leucine into protein,  $H^3$ -uridine into RNA, and  $H^3$ -thymidine into DNA 4 hours after initial exposure to actinomycin. One pair of cultures contained actinomycin D (0.2  $\mu$ g/ml), the other served as control. While the incorporation of leucine into protein and of thymidine into DNA were not affected by the antibiotic, uridine incorporation into RNA was depressed. After 24 hours, uridine uptake into RNA of the cells growing in the presence of actinomycin was still further decreased relative to the control.

The effect of actinomycin on virus growth has also been investigated. In some experiments cells had been treated previously with appropriate concentrations of the antibiotic, while in others

Table 1. Incorporation of precursors into protein, RNA, and DNA\*

Compound	Control	Actinomycin treated
Leucine- $H^3$ into protein	50,980	49,620
Uridine- $H^3$ into RNA	160,500	66,500
Thymidine- $H^3$ into DNA	194,000	181,000

\* Values expressed as total counts per minute for infinitely thin platings of equal aliquots obtained as follows: one pair of replicate cultures incubated in Eagle's medium containing 0.2 mmole of L-leucine received DL-leucine- $H^3$  (1  $\mu$ Ci/ml) and thymidine- $H^3$  (0.5  $\mu$ Ci, 0.4  $\mu$ g/ml) and the second pair uridine- $H^3$  (0.5  $\mu$ Ci, 0.8  $\mu$ g/ml). One culture of each pair was exposed to actinomycin (0.2  $\mu$ g/ml) for 30 min before and 3½ hours after addition of labeled compounds. Samples of 25 ml each were centrifuged and carriers added; they were then washed with phosphate-buffered saline, extracted with cold 0.25N  $HClO_4$  for 1 hour, and washed with ethanol and ethanol-ether. For leucine and thymidine determinations the washed pellets were hydrolyzed in 0.5N  $HClO_4$ , washed with ethanol and ethanol-ether and the pellets and hydrolysates were counted. For uridine measurement the pellets were incubated with ribonuclease (150  $\mu$ g/ml) for 2 hours at 37°C in .005M tris buffer, pH 8, made 0.2N with  $HClO_4$ , centrifuged, and the supernatant was counted.

actinomycin was present throughout the period of virus absorption and growth. The results were independent of the type of exposure.

The multiplication of vaccinia, a DNA virus, is sensitive to actinomycin, but somewhat less so than division of the host cell: 0.1  $\mu$ g/ml inhibited vaccinia growth by 99 percent, whereas 0.005  $\mu$ g/ml suppressed host cell division. On the other hand, concentrations of actinomycin in as high as 10  $\mu$ g/ml did not inhibit the growth or affect the yield of Mengo virus, a ribonucleic acid virus.

Parallel findings have been obtained with mitomycin, high concentrations of which inhibit cellular but not viral RNA synthesis (9). Whereas mitomycin appears to affect RNA synthesis by destroying the genes under whose control the various cellular RNA species are synthesized, actinomycin would seem to leave the genetic apparatus intact since DNA replication is not abolished. This is supported by studies on the effects of actinomycin S on phage synthesis (10). The inhibition of T2-phage reproduction by actinomycin does not result in inhibition of DNA synthesis in the phage-infected cell, whereas no phage protein appears to be made. Actinomycin thus appears to block the expression of genetic potentialities by interfering with that portion of RNA synthesis which is dependent on or governed by cellular or viral DNA. This is, therefore, a second line of evidence serving to differentiate replication of viral RNA from that of



cellular RNA. Reduplication of viral RNA is not necessarily inhibited by factors capable of interfering with RNA synthesis which is governed by viral or host DNA. Presumably, therefore, the two RNA synthetic processes are enzymatically or topographically distinct (11).

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21 June 1961

### Rapid Development of Drug-Resistant Mutants of Poliovirus

**Abstract.** Guanidine hydrochloride is a potent inhibitor of poliovirus synthesis in cell culture. However, the viral progeny which do grow in the presence of guanidine may become approximately 10,000 times more resistant to the drug. The phenomenon of drug resistance poses yet another problem in the search for a satisfactory viral chemotherapeutic agent.

Because guanidine is a potent inhibitor of poliovirus multiplication in tissue culture (1, 2), we tested the drug on monkeys infected orally with poliovirus (3). This provided us with virus which had multiplied in vivo in the presence of guanidine. In the present report we wish to call attention to the fact that when virus highly susceptible to the drug is grown in the presence of the drug either in vitro or in vivo, the progeny of the virus become drug resistant.

**Resistance produced in vitro.** Wild Mahoney poliovirus was carried for five passages in monkey kidney tube cul-

tures in the presence of guanidine hydrochloride; MG<sub>1</sub> and MG<sub>2</sub> are abbreviations for Mahoney passed once and five times, respectively, in the presence of guanidine. Controls passed in aliquots of the same cultures but in the absence of guanidine were labeled MC<sub>1</sub> and MC<sub>2</sub>. Increasing concentrations of guanidine from 20 µg/ml to 75 µg/ml (at the fifth passage) were used.

At each passage the viruses were harvested when over 75 percent of the cells were showing pathologic changes, and 0.1 ml was transferred to new cultures. Table 1 shows that virus many thousand times more resistant than the original virus has been obtained by selecting out guanidine-resistant variants. Since the first passage specimen already contained virus which was considerably more resistant than controls, it appears that a selection of spontaneously occurring mutants occurred in the first few cycles of multiplication in the presence of the drug.

Attenuated LSc strain, the very virus used in the oral polio vaccine, was treated in a similar manner. Again the first and fifth passage materials were found to be considerably more resistant to guanidine, the results being similar to those shown in Table 1.

**Resistance produced in vivo.** Cynomolgus monkeys fed three times daily with guanidine hydrochloride at near toxic levels (60 to 80 mg/kg per day) and fed virulent type 1 Mahoney poliovirus 3 days after the initiation of the drug course developed paralysis about as frequently as monkeys not treated with guanidine (3). On the 5th day after virus feeding, which was the 8th day of drug administration, virus was isolated from the blood of two monkeys. The resistance of these viruses to guanidine was compared with that of the original virus. The recovered progeny strains were grown in cultures free of guanidine before their drug resistance was measured.

A plaque titration was done with the above samples with an overlay containing 28 µg of guanidine per milliliter (2). One set of controls was set up containing the progeny viruses with normal overlay. A further set of controls included Mahoney virus from the same sample as that used in inoculating the monkeys. The original virus was inhibited 100 to 1000 times more than either of the viruses which had multiplied in the monkeys fed guanidine. Plaques of resistant virus under an

Table 1. Emergence of mutants of poliovirus resistant to guanidine hydrochloride. PFU, plaque-forming units; MC<sub>1</sub>, MC<sub>2</sub>, Mahoney virus passed one and five times, respectively, in control cultures without guanidine; MG<sub>1</sub>, MG<sub>2</sub>, Mahoney virus passed one and five times, respectively, in the presence of guanidine.

Concn. of drug in overlay (µg/ml)	Titers of virus (PFU/ml)			
	MC <sub>1</sub>	MG <sub>1</sub>	MC <sub>2</sub>	MG <sub>2</sub>
30	<10 <sup>2</sup>	10 <sup>5.7</sup>	<10 <sup>2</sup>	10 <sup>6.3</sup>
None	10 <sup>7.7</sup>	10 <sup>7.5</sup>	10 <sup>8.0</sup>	10 <sup>7.8</sup>

overlay of 28 µg of guanidine per milliliter were picked and passed in tube cultures without guanidine. On subsequent titrations this virus was found to be as resistant as before, indicating that the property is stable for several cycles of multiplication in the absence of guanidine.

**Comment.** Strains of poliovirus have been produced that are over a thousandfold more resistant to guanidine than the original viruses. The mechanism of the resistance is unknown. Nevertheless, the development of resistance to guanidine by poliovirus may be likened to the development of resistance to chemotherapeutic agents by certain bacteria, and it creates a potential difficulty in the development of an efficient viral chemotherapeutic agent.

The production of resistant strains which are easily distinguished from the parent strain offers a useful tool in the study of viral genetics. The fact that drug-resistant strains were as readily selected from progeny of an attenuated vaccine strain as from progeny of a wild strain emphasizes again the genetic pliability of the polioviruses (4, 5).

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6 April 1961

## Antiviral Effect of Guanidine

**Abstract.** It has been found that soluble guanidine salts show an antiviral effect on poliovirus and on some other enteroviruses. The activity was first detected in a cell culture screening system when the guanidine salt of hydroxyaminomethylene malononitrile inhibited the cytopathic effect of poliovirus in cell cultures. The studies were extended to various *in vivo* experiments in which the suggestive therapeutic activity of guanidine salts was again observed in monkeys infected with poliovirus. While these drugs cannot be considered for use in human disease because of severe toxicity, it is significant that potential antiviral compounds detected by the cell culture test show *in vivo* activity and point to the validity of such direct chemotherapeutic trials.

A tissue culture procedure has been developed which gives a semiquantitative estimate of the antiviral activity and cytotoxicity of chemotherapeutic agents in a single assay with the same cell culture (1). During the course of antiviral studies with this method, it was found that certain guanidine salts inhibited the cytopathic effect of poliovirus in mammalian cell cultures.

The antiviral activity was initially observed with the guanidine salt of hydroxyaminomethylene malononitrile (SV-870) (2) on type 2 poliovirus

(MEF-1) with No. 2 human epithelial (H.Ep. 2) cells as the cell culture system. The effect of this compound was demonstrated by infecting cultures with 1000 TCID<sub>50</sub> doses of virus and immediately treating with known decreasing concentrations of SV-870. The mixtures of virus, cell, and drug were incubated at 37°C for 7 days, at which time the cell monolayers were examined microscopically.

The drug was toxic to the H.Ep. 2 cells at 630 µg/ml, but inhibited the cytopathic effect of poliovirus at non-toxic concentrations of 200 and 63 µg/ml. The compound was inactive at 20 µg/ml. Subsequent testing of this type was done with simpler guanidine salts, since it was shown that guanidine hydrochloride at a concentration of 60 µg/ml in cell culture reduced the infectivity titer of poliovirus 10<sup>4</sup> to 10<sup>5</sup>-fold. Other guanidine salts showed activity that was approximately proportional to the solubility in the medium.

Delayed treatment of cultures infected with poliovirus showed that there was protection of cells when the monolayer was treated with SV-870 as long as 48 hr after exposures of cells to virus. In an application of a plaque-inhibition technique (3), a group of 48

cell cultures (in 32-oz bottles) was infected with 100 plaque-forming units (PFU) of type 1 (Mahoney) poliovirus, and a similar group of 48 bottles was inoculated with 1000 PFU doses of virus. After the virus was permitted to adsorb for 1 hr at 37°C, the cultures were washed once with 100 ml of media in order to dilute and remove the virus inoculum. The bottles were held at 37°C with 50 ml of maintenance media, and at intervals of 0, 1, 2, 8, 20, 30, and 48 hr six bottles of each group were removed and an agar overlay was added. Three of the bottles received an agar overlay containing 0.5 mg/ml of drug, and three received an overlay without drug. All cultures were held for 7 days, and the plaques from each group of bottles were totaled. There were no plaques in any culture in which the compound was incorporated in the agar overlay. In untreated controls at the 20- and 30-hr intervals, there was a total of 120 plaques and more than 500 plaques in cultures inoculated with the 100- and 1000-PFU dosages, respectively.

The guanidine salts have a limited spectrum of antiviral activity. Among a number of viruses studied in cell culture, the compound was effective against only members of the enterovirus groups, as shown in Table 1. Viruses not inhibited by guanidine salts were: (i) myxovirus-influenza A2 (Asian), parainfluenza 1 and 3 (Sendai and HA-1); (ii) herpesvirus-human and simian (HF strain and B virus, Yale strain); (iii) measlesvirus (Edmonston strain); (iv) poxvirus-vaccinia (CL strain); (v) arbovirus A-eastern equine encephalomyelitis (Massachusetts strain), arbovirus B-St. Louis encephalitis (Hubbard strain) and Japanese B encephalitis (Nak. strain); (vi) reovirus-Echo 10 (Lang strain); (vii) polyoma virus (Stewart-Eddy strain).

The chemotherapeutic effect of these compounds was studied in monkeys infected with poliovirus. The combined results from four experiments with guanidine hydrochloride and from three experiments with SV-870 are given in Table 2. In these studies *Macaca mulatta* (rhesus) monkeys, weighing from 2.0 to 4.5 kg, were challenged intramuscularly with type 1 (Mahoney) poliovirus in the left gastrocnemius muscle. The drugs were administered orally in one dose at daily intervals. The treatment schedule was initiated 3 days before virus challenge and con-

Table 1. Antiviral activity of SV-870.

Virus tested	TCID <sub>50</sub> virus titer with drug levels (mg/ml) at					
	Control (no drug)	0.015	0.03	0.06	0.125	0.250
Poliovirus, type 1 (Mahoney)	10 <sup>-8.5</sup>	10 <sup>-8.0</sup>	10 <sup>-7.5</sup>	10 <sup>-5.5</sup>	<10 <sup>-5.0</sup>	<10 <sup>-5.0</sup>
Poliovirus, type 2 (MEF-1)	10 <sup>-7.5</sup>	10 <sup>-6.5</sup>	10 <sup>-5.5</sup>	10 <sup>-4.5</sup>	<10 <sup>-4.5</sup>	<10 <sup>-4.5</sup>
Poliovirus, type 3 (Saukett)	10 <sup>-7.5</sup>	10 <sup>-6.9</sup>	10 <sup>-6.2</sup>	10 <sup>-5.0</sup>	<10 <sup>-5.0</sup>	<10 <sup>-5.0</sup>
ECHO-6 (D'Amori)	10 <sup>-7.3</sup>	10 <sup>-7.0</sup>	10 <sup>-6.0</sup>	10 <sup>-4.0</sup>	<10 <sup>-4.0</sup>	<10 <sup>-4.0</sup>
ECHO-9 (Bourn)	10 <sup>-8.0</sup>	10 <sup>-8.2</sup>	10 <sup>-7.8</sup>	10 <sup>-7.0</sup>	10 <sup>-6.8</sup>	10 <sup>-6.5</sup>
Coxsackie A-9 (Grigg)	10 <sup>-8.7</sup>	10 <sup>-8.5</sup>	10 <sup>-8.3</sup>	10 <sup>-6.7</sup>	10 <sup>-6.0</sup>	<10 <sup>-6.0</sup>
Coxsackie B-1 (Connecticut-5)	10 <sup>-6.8</sup>	10 <sup>-6.3</sup>	10 <sup>-5.9</sup>	10 <sup>-5.5</sup>	<10 <sup>-5.5</sup>	<10 <sup>-5.5</sup>

Table 2. Effect of guanidine salts administered orally to rhesus monkeys challenged intramuscularly with type 1 (Mahoney) virus.

Daily dose of drug (mg/kg)*	No. tested	Toxicity		No. satisfactory for polio test	Pathology typical of polio	
		Total	%		Total	%
<i>Guanidine hydrochloride</i>						
10-20	11	0	0	11	11	100
30-50	23	2	9	21	13	62
60-75	12	2	17	10	5	50
120-240	12	6	50	6	1	17
Control (no drug)	23			23	19	83
<i>SV-870</i>						
12-25	8	0	0	8	5	63
33-50	24	3	13	21	9	23
100	6	2	33	4	0	0
Control (no drug)	13			13	10	77

\*Values are the calculated amount of free guanidine base administered.

tinued 14 days after challenge for a total of 17 daily doses. Since clinical observations would not permit clear-cut differentiation between poliovirus infection and drug toxicity, the evaluation of the results was based upon the histopathological analysis of spinal cord and brain stem sections. There is an indication that both drugs were effective in decreasing the incidence of disease in the polio-infected monkeys, although the activity was seen only at marginal toxic levels.

It is significant that, in additional experiments in which the drugs were administered intramuscularly to monkeys at near toxic levels, no sparing effect similar to that seen with oral treatment was noted. In a limited study the activity of the drugs was not altered or enhanced by the oral administration of these compounds in divided dosages when compared with the same total dose at a single daily interval.

The evidence indicates that the effective agent is guanidine itself and not a derivative. Chromatographic studies were used to follow the fate of 2-C<sup>14</sup> guanidine hydrochloride when it was administered orally in mice. The animals were given radioactive guanidine corresponding to 20  $\mu$ c of activity, and then samples of blood, feces, and urine were taken at various intervals after administration of the compound. Two-dimensional paper chromatograms were prepared, and autoradiograms showed that the drug was adsorbed and excreted rapidly as unaltered guanidine with the urine containing many times more guanidine than either blood or feces. There was no apparent conversion of guanidine to other compounds.

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6 March 1961

## Foliar Retention of Strontium-90 by Wheat

**Abstract.** Wheat harvested from the University of Maryland Agronomy Farm in June 1959 contained 20 to 50 micro-microcuries of strontium-90 per kilogram of grain. More than 90 percent of the strontium-90 came from deposition on aboveground plant parts, and less than 10 percent was taken up through the soil. About 1 to 2 percent of the strontium-90 fallout during the time the heads were exposed was retained in the grain.

In order to further understanding of the mechanisms contributing to strontium-90 contamination of plants, Russell (1) has suggested the consideration of two components, one of which is absorbed through leaves, stems, and surface roots after lodging on them. The other component is absorbed through roots after incorporation into the soil. Specific activity measurements are helpful in separating the two components under natural fallout conditions, since the Sr<sup>90</sup> deposited in fallout is essentially carrier-free, while that which is incorporated into the soil is diluted by the exchangeable strontium in the soil.

Specific activity determinations were made on four samples of mature winter wheat plants collected on 17 and 18 June 1959 from the University of Maryland Agronomy Farm, Beltsville, Md.

Three samples were of the Leapland variety and one of Knox. The plants were separated into chaff, grain, leaves, stems, and roots, the roots being obtained from the surface 4 in. of soil and thoroughly washed with tap water to remove the soil adhering to them. The samples were dry ashed and dissolved in HCl. Calcium was determined in a small portion of the sample by titration with ethylenediaminetetraacetic acid, following double precipitation as calcium oxalate to remove interfering amounts of phosphate. Strontium was determined in the same portion by flame photometry. Strontium-90 was determined in the main part of the sample by separating and counting its radioactive daughter yttrium-90 (see Table 1).

The flame photometric strontium determination was not sensitive enough to detect the strontium content of the grain. While each plant sample contained a total of 5 to 10 mg of strontium, the grain contained less than 0.15 mg of strontium. This is in the lower range of results reported by Duckworth and Hawthorn (2), who showed that the grain contained 2 to 5 percent of the total Sr<sup>90</sup> taken up by wheat plants grown in sand culture. Our analyses showed much lower strontium-calcium ratios in the grain than in other parts of the plant, which indicates a marked discrimination

Table 1. Content of Ca, Sr, and Sr<sup>90</sup> in wheat plants harvested on University of Maryland Agronomy Farm, 17 and 18 June 1959. Samples A, C, and D were Leapland variety; sample B was Knox variety.

Sample	Wt. (g)	Ca (g)	Sr (mg)	Sr <sup>90</sup> ( $\mu$ mc)	Specific activity ( $\mu$ mc/mg)	Calculated Sr <sup>90</sup> from the air (%)
<i>Chaff</i>						
A	293	0.19	0.39	128	328	93
B	374	0.34	0.71	211	297	91
C	434	0.47	1.87	217	116	80
D	264	0.30	1.61	124	77	70
<i>Grain</i>						
A	1029	0.44	<0.09	22	>245	>90
B	1515	0.66	<0.14	80	>570	>95
C	1666	0.73	<0.12	61	>510	>95
D	974	0.39	<0.08	28	>350	>93
<i>Leaves</i>						
A	175	0.62	1.24	368	297	92
B	178	1.02	1.76	351	199	87
C	286	1.54	2.68	494	184	88
D	189	0.93	2.60	304	117	80
<i>Stems</i>						
A	556	0.54	1.96	126	64	62
B	496	0.86	3.00	175	58	55
C	714	1.04	4.83	187	39	41
D	528	0.73	3.34	97	29	21
<i>Roots</i>						
A	54	0.08	0.67	16	24	
B	63	0.14	0.95	25	26	
C	39	0.10	0.78	18	23	
D	59	0.11	0.77	18	23	



against strontium relative to calcium in the formation of wheat grain.

The specific activity of strontium was highest in the grain, and next highest in the chaff and leaves. It was about one-fifth as high in the stems and one-tenth as high in the roots. It is natural to assume that the specific activity of strontium in the roots equals that of strontium taken up from the soil. However, soil contamination on the root samples might lower the specific activity by adding stable strontium. On the other hand, since the root sample was taken near the surface, it is possible that its strontium would have a higher specific activity than the average for strontium taken up from the soil. These errors are expected to be small and they tend to offset each other. It is thought that the specific activity of strontium in roots gives a fairly good estimate of that taken up from the soil. This value was used in Table 1 to calculate the percentages of  $\text{Sr}^{90}$  absorbed through the aboveground parts.

All exposed parts showed a major fraction of  $\text{Sr}^{90}$  deposited directly from the atmosphere. In the grain, over 90 percent of the  $\text{Sr}^{90}$  entered by deposition on exposed parts and less than 10 percent by way of the soil. Other data on fallout in Maryland (3) indicate that the soil level in March 1959 was about  $80 \mu\text{C}$  of  $\text{Sr}^{90}$  per acre, and that fallout during April, May, and June was about 9, 3, and  $3 \mu\text{C}/\text{acre}$ , respectively. Thus, fallout was about  $15 \mu\text{C}/\text{acre}$  during the spring growing season and about  $3 \mu\text{C}/\text{acre}$  during the time the wheat heads were exposed.

The retention of  $\text{Sr}^{90}$  fallout by wheat plants and grain may be estimated as follows. The average  $\text{Sr}^{90}$  content of the grain was  $35 \mu\text{C}/\text{kg}$ . Based on an estimated yield of 40 bu/acre, the  $\text{Sr}^{90}$  content of the grain averaged  $0.038 \mu\text{C}/\text{acre}$ , of which more than  $0.035 \mu\text{C}$  was direct deposition. Thus, the grain contained about 1 percent of the  $\text{Sr}^{90}$  deposited while the heads were exposed, and absorbed about 0.004 percent of that in the soil. Similarly, the whole crop contained  $0.63 \mu\text{C}/\text{acre}$ , of which  $0.49 \mu\text{C}$  was direct deposition. Thus, the whole crop retained about 3 percent of that deposited during the growing season, and took up about 0.2 percent of that in the soil (4).

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29 March 1961

### Single Unit Activity of Anterior Hypothalamus during Local Heating

**Abstract.** There are heat-sensitive units in the anterior hypothalamus which respond with an increase of discharge frequency to a rise in hypothalamic temperature of less than  $1^\circ\text{C}$ . The increase of unit discharge occurred in advance of the onset of polypnea, and the unit has little phasic response or after discharge, and shows little adaptation.

Hypothalamic involvement in the mechanism of body temperature regulation is now generally accepted. Numerous experiments have been done and most of them indicate that a thermally sensitive area is located in the anterior hypothalamus. By local radio-frequency heating of the ventral telencephalon, between the anterior commissure and the base of the brain, Magoun *et al.* (1) demonstrated a marked acceleration of respiratory rate and the appearance of sweat on the foot pads. Polypneic panting and

cutaneous vasodilatation have also been induced in unanesthetized animals either by local electrical stimulation at 50 cy/sec (2) or by warm water circulation of the hypothalamus (3). With lesions in the anterior hypothalamus, animals do not react to a rise of environmental temperature (4). Electrophysiological approaches to the hypothalamic temperature-sensitive neurones have so far been rather limited. C. von Euler (5) recorded slow potential changes from the hypothalamus which correlated with the occurrence of heat polypnea and panting. In view of the above, an experiment was designed to record single neuron activity in the hypothalamus during local heating.

Cats were anesthetized with urethane in doses of 1.2 g/kg of body weight. (In some cases urethane itself induced polypnea for an hour or more.) Tungsten or steel electrodes, with exposed tips of about  $1 \mu$ , were inserted stereotactically into the anterior hypothalamus. For radio-frequency heating, two thermodes, insulated except for 4 mm at the tip, were implanted in the brain substance to within 1 mm of the base of the skull at the level of the anterior commissure and 4 mm on either side of the mid-line. The frequency of the low-voltage heating current, applied to the hypothalamus through the two thermodes, was 3 Mcy/sec. The duration of stimulus was usually less than 3 min. Conductive warming with a water circulator (3) was also used.

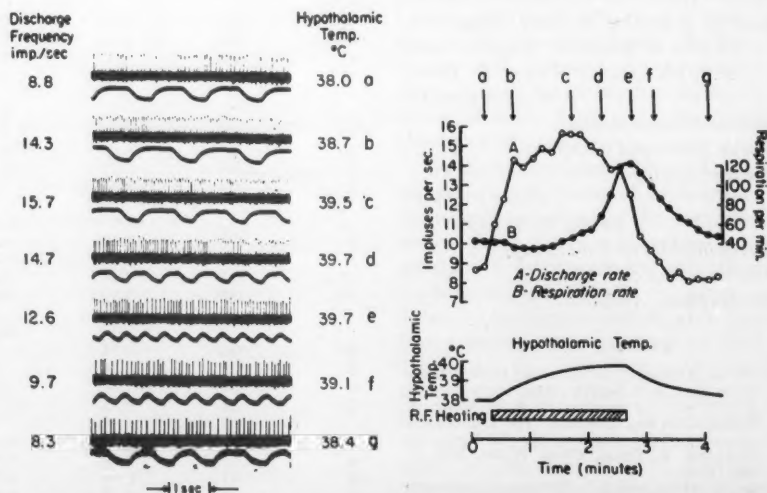


Fig. 1. Effect of local radio-frequency heating of the anterior hypothalamus on electric activity of single cell and respiration.



Rectal temperature was monitored throughout the experiment and was kept in the normal range by a heating pad placed beneath the animal. The hypothalamic temperature was measured with a thermocouple, or estimated indirectly from measurements of the thermode temperature. Respiratory movements were picked up by a thermopile placed in the tracheal cannula and recorded on the face of an oscilloscope simultaneously with the neuron discharge.

The frequency of spontaneous unit discharges in the anterior hypothalamus ranged from 3.7 to 27 per second. The discharge of a particular cell was rather stable, firing at an almost constant rate for several minutes. Some units changed their discharge interval with the rhythm of respiration. Numerous units which did not respond to local heating were found in the anterior hypothalamus. Regardless of an increase in respiration rate at hypothalamic temperatures of even more than 40°C, the discharge frequencies of these units remained fairly constant. The existence of a unit which does not respond with increased frequency to heating serves as a good control for heat-sensitive units. A few units have been found in the anterior hypothalamus which respond to local heating with a slight decrease in frequency. Occasionally the amplitude of the discharge decreased or increased with heating and returned to the normal 1 or 2 min after cessation of heating without any change in frequency. This change of amplitude is thought to be brought about by tissue movement with respect to the electrode.

Units which increase their discharge frequencies during local heating have so far been found stereotactically in a region 13.5 to 15.5 mm rostral from the stereotaxic zero point, within 2 mm of the mid-line, and between 0.5 to 3 mm from the bottom of the brain tissue. The increase of frequency always occurred prior to the onset of polypnea, and even in an anesthetized cat an elevation of less than 1°C in the hypothalamic temperature was enough to increase significantly the discharge frequency. In an experiment in which the hypothalamic temperature was changed slowly by the circulation of warm water, the discharge frequency per second was 7.2, 15, and 21.2 at hypothalamic temperatures of 36.8°, 38°, and 38.7°C,

respectively. The discharge rate remained fairly constant and showed little adaptation at a given hypothalamic temperature so long as the intensity of heating was moderate. These thermally sensitive units did not stop firing but showed a minor decrease in frequency when the hypothalamic temperature was lowered to 32°C. One unit, however, had a minimum frequency at 35.4°C, and increased its frequency with either cooling or heating.

The relation between hypothalamic temperature, unit discharge, and respiration is illustrated in Fig. 1. With radio-frequency heating the hypothalamic temperature went up gradually and the discharge began to increase in frequency. The discharge reached its maximum frequency 80 sec after the beginning of heating and maintained a fairly constant frequency at this level. Coincident with the fall of hypothalamic temperature, the frequency of discharge decreased without showing any afterdischarge. Close inspection of this figure, however, reveals that the frequency decreased a little while the hypothalamic temperature was still rising. Such a tendency of decrease is more conspicuous at higher hypothalamic temperatures, and in this type of response the frequency usually decreased markedly in the recovery phase after cessation of heating and then returned to the starting level. During the first minute or so of the heating period the respiration rate remained fairly constant or, more frequently, decreased slightly, as shown in Fig. 1.

In another series of experiments, rapid heating was employed, that is, the hypothalamic temperature was raised 6.5°C in 24 sec, from 38°C to 44.5°C, in an attempt to see whether any phasic response could be evoked. The discharge rate, 9.5 per second at normal temperature, decreased suddenly to 6 per second 3 seconds after the beginning of temperature elevation and then increased and reached the maximum frequency of 28 per second in 31 sec. Other units which showed no initial inhibition responded to a rapid heating with a minor increase in frequency.

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2 May 1961

## Authigenic Dolomite in Modern Carbonate Sediments along the Southern Coast of Florida

**Abstract.** Crystalline authigenic dolomite in shallow-water marine sediments from the margins of the North American continent is described for the first time. Dolomite is probably forming at the water-sediment interface in Florida Bay because of an interaction between organic material and hypersaline sea water.

Dolomite crystals occur in carbonate sediments now accumulating in shallow sea water along the southern coast of Florida (latitude, 25° 05' 50" N; longitude, 80° 53' 58" W). Examination of sediment cores shows that dolomite is most abundant near the sediment-water interface. These dolomite crystals are associated with calcareous shell fragments that have accumulated to form carbonate mud banks which overlie the consolidated Miami oolite of Pleistocene age. Along the western margin of Florida Bay, where dolomite appears to be concentrated, the unconsolidated mud is approximately 1.5 m thick. During periods of low water the mud is exposed to the atmosphere.

The dolomite crystals are characteristically euhedral rhombohedrons, ranging in size from less than 1  $\mu$  to approximately 60  $\mu$ ; they commonly contain dark internal rhombohedrons that appear to be intergrowths of dolomite and dark material, possibly organic (Fig. 1). Clusters of interpenetrating rhombohedrons, in rare specimens, appear to be in the process of growth.

Unconsolidated carbonate sediment was leached with distilled water to remove all interstitial dissolved solids, filtered with Pasteur filter candles, passed wet through a screen with 62- $\mu$  openings, and suspended in a 2.5M solu-

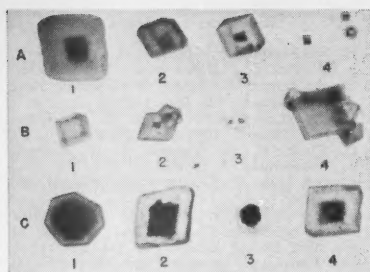


Fig. 1. Photomicrographs of typical dolomite crystals that occur in modern unconsolidated marine carbonate muds along the southern coast of Florida. Crystals range in size from about 16 to 62  $\mu$ , although the degree of enlargement varies from photograph to photograph. A-1, A-2, and A-3: euhedral crystals with dark organic material inside. A-4: three crystals contrasting lack of etching (lower two) with high degree of etching and loss of crystal faces (upper one). B-1: euhedral crystals lacking an inclusion. B-2, B-3, and B-4: interpenetrating euhedral crystals. C-1: seven-sided crystal that appears to be in initial growth stage. C-2, C-3, and C-4: euhedral crystals with rhombohedral-shaped dark inclusions.

tion of  $\text{Na}_2\text{CO}_3$ . The suspensions were decanted to effect a sizing based on settling velocity and particle size. Dolomite was suspected when rhombohedrons were found with an electron microscope in the size fraction of less than 1  $\mu$ . Many preparations, ranging in size between 62 and 16  $\mu$ , were acidified in very dilute (1:30) HCl to remove the

more soluble (in dilute acid) aragonite, calcite, and magnesian calcite that constitute more than 95 percent of the total carbonate. The insoluble residue was studied by x-ray diffraction on a Norelco high-angle Geiger-Mueller counter goniometer. As shown by Fig. 2, the insoluble residue consists of dolomite and quartz.

The origin of the dolomite is incompletely known. The presence of complex clusters of these crystals suggests that it has not been transported. The apparent concentration of dolomite near the top of the sediment cores suggests that dolomite is forming at the sediment-water interface rather than after burial in some diagenetic process. If exposure of the mud bank coincides with a time of high evaporation, concentration of the dissolved solids in the surface film of water will rise markedly. The presence of organic material and a high concentration of dissolved salts may possibly be the conditions necessary to initiate growth of the original dolomite crystal on which later crystals may grow.

Fairbridge (1) has reviewed the problem of the origin of dolomite. In brief, dolomite is an important constituent in ancient calcareous rocks, but is not known to be forming in modern carbonate sediments whose depositional environment is considered to be typical of ancient deposits. As shown by the present study, however, dolomite is

forming along the western margin of Florida Bay. Further geochemical study of this occurrence should help to clarify the origin of some ancient dolomites (2).

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15 May 1961

#### Mass Culture of Phytoplankton as Foods for Metazoans

**Abstract.** An apparatus for mass culture of photosynthetic microorganisms has been developed to grow algae for use as foods for larval and juvenile mollusks in studies of their physiological requirements. The apparatus consists of a series of 5-gal growth chambers, and the system can be enlarged to yield any desired volume of algae by replication of basic units. Approximately 50 lit. of algal suspension, averaging about 0.5 ml of packed wet cells per liter, are produced daily.

In developing a standard technique for rearing lamellibranch larvae, one of the requirements was to provide an adequate quantity of food. To be ingested by early-swimming larvae of the American oyster, *Crassostrea virginica*, food particles must be in suspension and must not be larger than about 7  $\mu$  in size.

Photosynthetic nanoplankton appeared to be the most promising natural food. It was found, however, that various species of microorganisms not only differ in food value, but that some are not utilized at all, while others are actually toxic (1, 2). Some produce toxins that appear to be intracellular but, more commonly, toxins occur as external metabolites. Certain bacteria also produce toxins (3). In low concentrations these toxins only retard the growth of bivalve larvae, but sometimes concentrations are sufficient to prevent development of eggs, or kill larvae (4).

To provide food for the daily feeding of the larval and juvenile mollusks at this laboratory, from 20 to 60 lit./day of a relatively dense culture of food organisms in unialgal and,

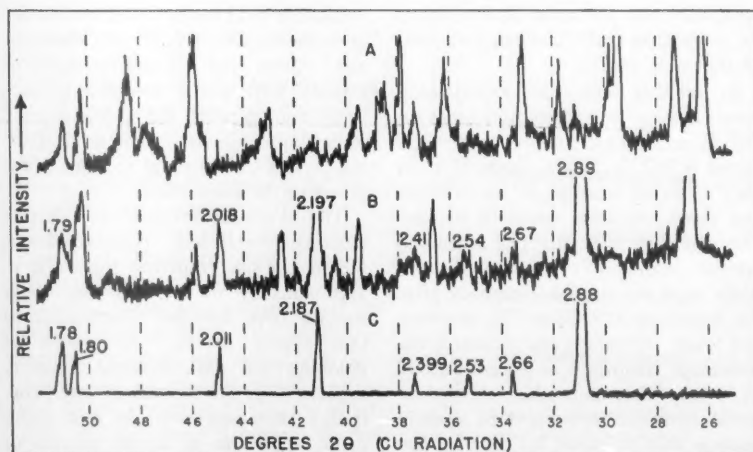


Fig. 2. Comparison of three x-ray diffraction patterns that confirm presence of dolomite in Florida carbonate muds. (A) Diffraction pattern of untreated carbonate mud. Note that no dolomite peak appears at 31°. (B) Diffraction pattern of residue of sample A after calcite, aragonite, and magnesian calcite have been leached away with dilute HCl. Note presence of strong dolomite peak at 31°. Also note that  $d_{hkl}$  values for dolomite peaks are listed; other peaks are quartz which also occurs in the residue. (C) Diffraction pattern of U.S. Bureau of Standards No. 88 standard dolomite shows dolomite peaks comparable to those in B.

preferably, bacteria-free culture are needed. For a pilot or commercial hatchery for clams or oysters this requirement could easily be from 100 to 1000 gal daily. The objective, therefore, was to develop a culture apparatus that is inexpensive, simple to operate, and capable of producing any desired volume of the food culture. A number of comparatively small basic units is preferable to a single larger unit, since several species of algae can then be produced simultaneously. This is important because a mixture of several species of microorganisms often causes better growth of larvae than any single species (2), and because larvae of different bivalves require different foods. Moreover, the best foods for larvae are not necessarily the best foods for juveniles of the same species.

Use of algae as food is not, of course, confined to bivalves and their larvae. There are filter-feeding representatives of almost every phylum of aquatic invertebrates that subsist on algae either during early stages of their development or throughout their lives. Development of a dependable method for growth and maintenance of mass cultures of algae is, therefore, a requirement for keeping large colonies of these aquatic animals healthy.

Our culture apparatus accommodates 16 5-gal Pyrex carboys or 20 9-lit. Pyrex serum bottles as growth chambers. Vigorous agitation, by bubbling a mixture of air and CO<sub>2</sub> through the cultures, keeps the contents of the chamber thoroughly mixed. This prevents stratification and helps to expose all cells to periods of intense illumination. The growth chambers are immersed to a depth of 3 or 4 inches in a water bath kept at  $19^{\circ} \pm 1^{\circ}\text{C}$  by a force-flow constant temperature unit. Lighting is provided by four 40-watt, cool-white fluorescent tubes situated behind the back row of growth chambers and three 40-watt tubes suspended above the front row (Fig. 1).

About 1.5 lit. of culture are withdrawn daily from each serum bottle growth chamber, or 3 lit./day from each carboy. Although the various species of algae differ in their rate of growth and final density maintained, some of our cultures have been maintained at this rate of productivity for more than a year, yielding about 0.75 ml of packed wet cells daily from each 9-lit. serum bottle, or 1.5 ml/day from each 5-gal carboy. A volume of sterile sea water and nutrient salts,

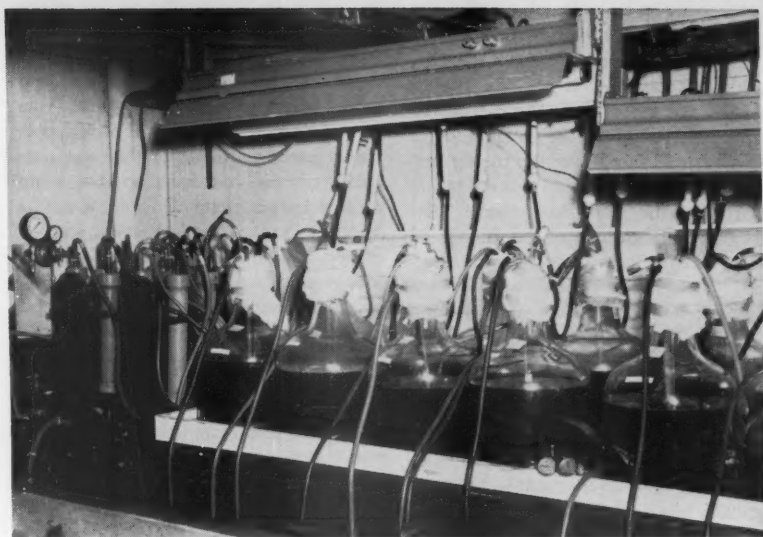


Fig. 1. Culture apparatus, showing carboy growth chambers in water bath and arrangement of lights.

equal to the volume of culture drawn off, is aseptically added to the growth chamber each day.

Mass cultures of chrysomonads, cryptomonads, chlorophytes, and diatoms have been grown successfully in our apparatus. They include *Isochrysis galbana*, *Monochrysis lutheri*, *Dicrateria inornata*, *Dicrateria* sp. (BII), *Chromulina pleiades*, *Phaeodactylum tricornutum*, *Cryptomonas* sp., *Dunaliella euchlora*, *Dunaliella primolecta*, *Chlorella* sp. (580), and *Skeletonema costatum*.

Much of the labor involved in older methods that use heat sterilization has been eliminated by using a "cold"

method of sterilization of the media added to the growth chambers. A number of "cold" methods of sterilization were tested but, until lately, none had proved satisfactory. Recently, by placing a ceramic filter (Selas No. FP-128-03) in the intake line for each growth chamber (Fig. 2), a satisfactory system has been developed. The sea water is first passed through "Ful-flu" Orlon filters to remove larger particles, nutrient salts are added, and this solution is forced through the ceramic filter (maximum pore size  $0.6 \mu$ ) to replace the culture drawn off.

The growth chamber and Selas filter, together with the tubing connecting

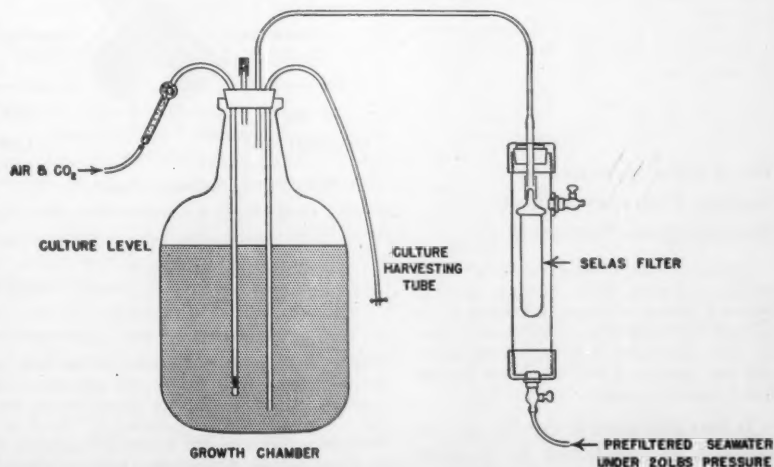


Fig. 2. Diagram of culture apparatus, which uses Selas filter for sterilizing sea water.



them, can be autoclaved already assembled. The casing, into which the Sels filter fits, is of polyvinyl chloride, and the stopcocks are of hard rubber and are not autoclaved. The cap at the upper end of the case is slotted so that it can be fitted over the tubing and stopper after the sterile Sels filter is inserted. This permits periodic disassembly and washing of the outside of the filter in hot water without disturbing the sterile system.

Occasionally growth of algae in enriched sea water is poor, either because of the absence of some essential nutrient normally present in sea water or because of the presence of some toxin. Some artificial sea waters, such as that used by Provasoli *et al.* (5), are satisfactory and give uniform results, but their use would be expensive and their preparation time-consuming if used for large-volume cultures. When the nutrient requirements of each of the species of algae under cultivation are known, it should be possible to add a complete nutrient mixture to sea water so that algal cultures will grow well at all times, except during those probably rare periods when toxic elements or metabolites are present in high enough concentrations to retard growth.

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14 March 1961

### Blood Flow Measured by Doppler Frequency Shift of Back-Scattered Ultrasound

**Abstract.** The Doppler shift of ultrasound, scattered from moving elements within a stream of blood, is related to the velocity of blood flow. A flowmeter based on this principle has been constructed and was used to record blood flow through intact vessels in dogs.

If two piezoelectric crystals (barium titanate) are positioned in a plastic cylinder so that they are directed toward a point in the center of the chan-

nel (Fig. 1), a sound beam of ultrasonic frequency (5 Mc/sec) generated from one crystal passes through pure water with so little scattering that no detectable sound energy reaches the second (receiver) crystal. Foreign particles, such as small bubbles or particles, provide interfaces so that some of the sound energy in the beam is scattered and a small fraction reaches the crystal on the opposite side. Normal blood produces sufficient scattering of a 2-watt/cm<sup>2</sup>, 5-Mcy/sec sound beam to provide a detectable level of sound energy at the receiver crystal. If the blood in the cylinder is stationary, the frequency of sound at the receiver crystal is precisely the same as the transmitted frequency. When blood flows along the cylinder, the frequency of the back-scattered sound is altered by the Doppler shift. Since the various particles move at different velocities across the stream, the frequency spectrum of the sound returning from the various interfaces is broadened. However, the frequency of the reflected signal, determined by the frequency meter, was found to be linearly related to the instantaneous flow velocity of the blood during both steady and sinusoidal flow. Thus, the mean Doppler shift in frequency can be employed as a measure of the instantaneous flow velocity of blood.

The plastic transducer was clamped about a length of thin-walled rubber

tubing; and the spaces between the crystals and tubing wall were filled with water to couple into the tubing. The received signal was mixed with the transmitted signal to develop a beat signal corresponding in frequency to the Doppler shift. The received frequency differed from the transmitted frequency by 0 to 3500 cy/sec as flow velocity varied from 0 to 100 cm/sec. All frequencies above 15 kcy/sec were rejected by a filter, and the signal was coupled to a frequency meter of the type which develops an analogue voltage proportional to the number of voltage zero crossings per unit time. The voltage from this frequency meter was found to be a linear indication of flow velocity within 5 percent of full scale deflection (100 cm/sec). Furthermore, zero flow levels could be quickly and reliably established by merely removing the voltage input to the frequency meter.

The plastic cylinder was clamped about an unopened artery (descending aorta) of an anesthetized dog, and the recorded signal produced a fairly typical pattern of arterial flow for this site. However, since this simple developmental device does not sense direction of flow, a transient retrograde surge of flow would not be detected. There is some danger that the sonic intensity required to produce detectable reflected sound energy at the receiver crystal may produce hemolysis. However, the

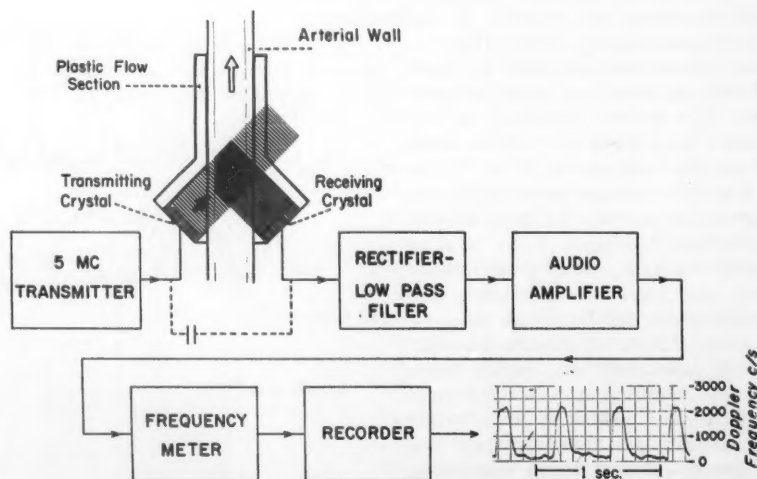


Fig. 1. A method of recording blood flow by measuring the Doppler shift in frequency of ultrasound scattered in the moving blood. High frequency (5 Mc/sec) sound is beamed diagonally into the blood stream where a part of the incident sound is scattered by the particulate components of blood to the receiving crystal. A beat note with a frequency equal to the Doppler frequency shift is developed from the transmitted and received signals. A frequency meter develops a d-c voltage proportional to the frequency of the beat note. This output voltage is recorded and calibrated in terms of flow. A wave form of flow through the intact descending thoracic aorta of a dog is illustrated.



component parts for the flowmeter cost less than \$100, it is extremely sensitive (about 3.5 cy/sec per millimeter of flow velocity per second), and zero flow level can be easily determined without interfering with actual flow through the vessel (1).

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#### Note

1. This work was supported in part by a grant (H-4531) from the National Heart Institute, National Institutes of Health, U.S. Public Health Service.

10 April 1961

### Eastern Equine Encephalomyelitis Vaccine Prepared in Cell Cultures

**Abstract.** Protection tests in guinea pigs indicate that vaccines prepared from virus propagated in chick embryo cell cultures are as effective as the purified whole chick embryo vaccines which are currently used for human immunization against eastern equine encephalomyelitis.

The extensive distribution of the virus of eastern equine encephalomyelitis, and the occurrence of an increasing number of human cases of this disease, have caused a renewed interest in the preparation of a vaccine for the immunization of those individuals who are exposed to this agent. In 1940, Randall described the preparation of a chick embryo vaccine, inactivated by 0.4 percent formalin, for the immunization of Army horses and mules located in known infected areas (1). Considering that for human use it was desirable to reduce the high content of chick tissue and egg components in this vaccine, Randall, Mills, and Engel, in 1947, described a method for purifying this vaccine involving a two-stage differential centrifugation and concentration (2). Since 1957 the purified chick embryo vaccine has been produced by the Department of Biologics Research, Walter Reed Army Institute of Research, for the immunization of laboratory personnel and exposed field workers. Most lots of this vaccine, freeze-dried for maximum stability, have been shown to protect a majority of guinea pigs against a challenge of 100 to 1000 intracerebral LD<sub>50</sub> doses of virus. Serum neutralizing antibody response of humans to an initial series of vaccine inoculations has varied from poor to good.

The use of cell culture methods for the cultivation of arthropod-borne viruses has suggested the possibility of the production of a vaccine against eastern equine encephalomyelitis from virus propagated in chick embryo fibroblast monolayers, rather than in the whole chick embryo. Such a system would result in a relatively pure vaccine without the need for differential centrifugation, a procedure which undoubtedly results in the loss of a considerable amount of viral antigen. This report presents the results of studies on the preparation of experimental vaccines from chick embryo cell cultures (3).

Primary cultures of fibroblasts from chick embryos 9 to 10 days old were prepared by seeding Povitsky bottles with 150 ml of trypsinized chick embryo cells ( $2 \times 10^6$  per milliliter) suspended in mixture 199, containing 2 percent calf serum and 100 units of penicillin and 50  $\mu$ g of streptomycin per milliliter at pH 7.4 to 7.6. Uniform monolayers were obtained after incubation at 36°C for 44 to 48 hours. The spent medium was decanted, and the monolayers were washed with 100 ml of Earle's solution containing antibiotics. After thorough draining of the wash solution, the cells were overlaid with 150 ml of a  $10^{-4}$  dilution of chick embryo suspension infected with eastern equine encephalomyelitis in mixture 199 (containing no serum or antibiotics); the bottles were then returned to the incubator. Disintegration of the cells as a result of viral action begins to occur after approximately 20 hours of incubation and is complete after an additional 6 to 10 hours. Since the maximum virus titer ( $10^{7.5}$  mouse intracerebral LD<sub>50</sub> doses per 0.03 ml) appears in the culture fluid after 20 hours of incubation, harvesting of the fluids at this point minimizes the contamination of the culture fluids by material from the damaged cells.

The pooled culture fluids were centrifuged at low speed (2000 rev/min for 30 min) to remove suspended tissue cells, and portions were then filtered through a Millipore filter (HA) to remove particulate matter. Viral titrations in mice indicate that these procedures can be accomplished with less than 0.5 log reduction in virus titer. The virus is inactivated by the addition of neutral formalin to a final concentration of 0.05 percent and by storage of the mixture, with frequent shaking, at 22°C for 4 days and then at 5°C for an additional 10 days. Studies on the rate of inactivation by formalin demon-

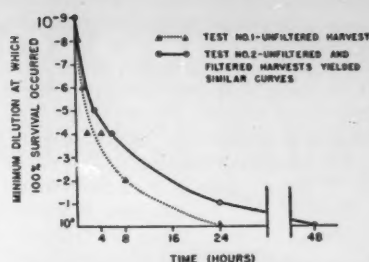


Fig. 1. Inactivation of chick embryo cell culture propagated eastern equine encephalomyelitis virus by 0.05 percent formalin at 22°C, as measured by intracerebral inoculation of white mice.

strated that no active virus could be detected after 48 hours at 22°C when 0.03 ml of the undiluted vaccine was inoculated intracerebrally into each of 20 mice (Fig. 1).

For those preparations which were freeze-dried, the formalin was neutralized with sodium bisulfite after the inactivation period and the product was freeze-dried in a chamber dryer. Inoculation of 0.03 ml of the fluid or rehydrated final product intracerebrally into each of 50 white mice failed to detect any live virus. Sterility and toxicity tests were also satisfactory. Potency tests in guinea pigs demonstrated that the cell culture vaccines are at least as effective as the chick embryo vaccines in protecting the animals against an intracerebral challenge of 100 to 1000 LD<sub>50</sub> doses of virus (Table 1).

Sufficient encouragement is derived

Table 1. Protection of guinea pigs immunized with eastern equine encephalomyelitis vaccine against intracerebral challenge with 100 to 1000 intracerebral LD<sub>50</sub> doses of virus (S/T, number of survivors per total number challenged).

Lot	Type of vaccine			
	Fluid		Dried	
	S/T	%S	S/T	%S
<i>Whole chick embryo vaccine (purified)</i>				
R-A	3/6	50	2/6	33
R-B	5/6	83	4/6	67
R-C	4/6	67	—	—
R-D	—	—	4/6	67
R-E	9/15	60	11/21	52
Total	21/33	64	21/39	54
<i>Cell culture vaccine (unfiltered)</i>				
CC-A	6/6	100	—	—
CC-B	5/6	83	5/6	83
CC-C	9/10	90	9/10	90
CC-D	6/6	100	—	—
CC-E	5/6	83	4/6	67
CC-F	5/6	83	5/6	83
Total	36/40	90	23/28	82
<i>Cell culture vaccine (filtered)</i>				
CC-D	4/6	67	—	—
CC-E	4/6	67	4/6	67
CC-F	5/5	100	5/6	83
Total	13/17	76	9/12	75

from data for laboratory animals to justify further study of a vaccine prepared from virus propagated in chick embryo cell cultures, for use in the immunization of humans against eastern equine encephalomyelitis.

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3. The excellent technical assistance of Miss Mette Strand and Mrs. June Cole is acknowledged.

9 May 1961

### Calcification of the Permanent First Mandibular Molar in Rhesus Monkeys

**Abstract.** Evidence suggests that in rhesus monkeys calcification in the mandibular permanent first molar commences much earlier than has been previously reported. This tooth is the first secondary dental element to calcify, as it is in man.

To my knowledge there are no studies relating directly to the calcification of either the deciduous or permanent teeth in the rhesus monkey. Perhaps the only exception to this is in the widely used *Anatomy of the Rhesus Monkey* (1933), which has recently been reprinted (1). In the chapter on the teeth, Marshall discusses rather briefly the complex problem of tooth calcification. Because of the obvious importance this subject has for the dental researcher, and since there are several inconsistencies in Marshall's presentation, it seems appropriate to present some new observations on the calcification of the permanent first mandibular molar.

In his study of the development of the deciduous and permanent teeth, Marshall made the following comments:

1) In still-born animals of a gestation period ranging from 153 to 169 days, x-rays indicated, "The calcification of the deciduous second molars and of the permanent first molars is just beginning" (1, p. 85).

2) In 14 animals between 1 and 2 months old, "There was no evidence at

this age of even the beginning of calcification of the permanent teeth" (1, p. 85).

3) "The calcification of the second set of teeth was not demonstrated roentgenographically until after the sixth month. At this time the permanent upper central incisors are just beginning to be formed" (1, p. 86).

It seemed advisable, therefore, to re-examine these statements in the light of our observations in the developing deciduous and permanent teeth of rhesus monkeys.

To date, 13 animals have been born in our colony at Charleston. Of these 13 animals, four had x-rays taken on the day of birth, whereas the initial x-rays of the other animals were taken at various ages (see Table 1). One male rhesus fetus of approximately 129 days gestation (170 days average gestation period) (2) was dissected, cleared, and stained with alizarin red S, the method of Noback and Noback (3) being used.

Table 1 presents the findings on the live animals via roentgenography. For two animals the lower molar is listed under "questionable," because the identification was not positive. I believe that the crown tips are present; however, I prefer to record the animals in the "not sure" category. Animal number 109 did not have jaw films taken again until he was 1 year old, at which time the permanent first mandibular molar was well formed. Number 119 was 1 day old at the time this report was written. It should be mentioned that No. 113 has a large, well-formed crown which is clearly visible on the x-ray film. It is evident, therefore, that the present x-ray evidence does not substantiate statements 2 and 3 of Marshall; on the contrary, it suggests a much earlier calcification time for the permanent first mandibular molar, more in line with Marshall's first pronouncement. Incidentally, I have never observed calcification occurring in the permanent maxillary central incisors earlier than in the permanent first mandibular molars, as noted by Marshall in his statement 3. The present findings indicate that the permanent first mandibular molar is the first permanent tooth to calcify, and in this respect the rhesus monkey is similar to man.

The fetal monkey that was dissected would seem to confirm this. While all the deciduous teeth were present and well developed morphogenetically, the

Table 1. Calcification of permanent first mandibular molar. In column three, zero indicates that the first x-ray was made at birth.

Animal No.	Sex	Postnatal age at first x-ray (days)	Lower molar
108	F	14	Present
110	F	21	Present
112	F	0	Present
117	M	14	Present
104	F	32	Present
106	F	44	Present
109	M	3	Questionable
111	M	113	Present
113	M	170	Present
115	M	56	Present
119	M	0	Questionable
121	M	0	Present
114	F	0	Present

crypts for the mandibular and maxillary permanent first molar were discovered. The crypts for the upper molars contained only a membranous dental organ at a stage preceding the formation of hard structures, whereas the mandibular crypts had the membranous dental organ with two of the four crown tips beginning to calcify. X-rays were unable to detect this early formation of calcified material but alizarin red S was absorbed by these minute cusp tips. (For a more elaborate comment relating to this question, see 4.) These primordial dental organs were characterized by their bilophodont appearance, two mesial and two distal cusps connected by a transverse ridge (5). The two calcified cusps would correspond to the mesial buccal (protoconid) and distal buccal (hypoconid) cusps of dental terminology. It is interesting to note that Kraus found the mesial buccal cusp the first to calcify in his investigations of human teeth (6, 7).

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7. This research was supported by grants (C-2663 and H-2417) from the U.S. Public Health Service.

1 May 1961

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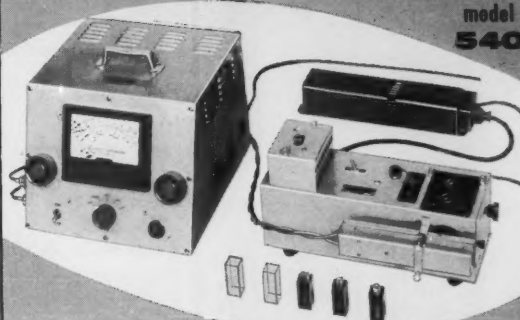
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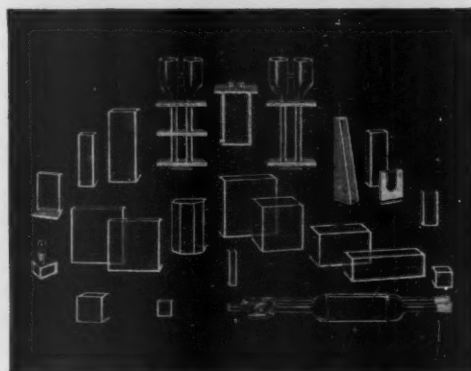
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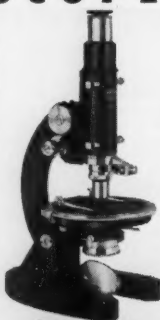
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## Meetings

### International Andean Year

On the initiative of UNESCO and by invitation of Angel Establier (head of the organization's Scientific Office in Latin America, located in Montevideo), who was interested in this project from its very beginning, a meeting was held in Buenos Aires on 3 and 4 April 1961 to discuss the planning of an International Andean Year, during which an intensive study would be carried out on the range of mountains known as the Cordillera de los Andes, which extends from Panama to the southern part of the Continent.

Scientists from various interested countries participated in the meeting—H. O'Reilly Sternberg (Brazil); Guillermo Mann (Chile); Tobías Lasser (Venezuela); Ovidio Suarez (Bolivia); and Eduardo Baglietto, M. Olasoaga, F. Bonorino Udaondo, J. Roederer, Angel Cabrera, M. Sadosky, B. A. Houssay, and V. Deulofeu, all from Argentina. Unfortunately, A. Hurtado, from Peru, could not attend the meeting. Angel Establier represented UNESCO, and his office will be the center for the various groups in preparing the project.

After a few words of welcome by M. Sadosky, vice-dean of the faculty of exact and natural sciences, University of Buenos Aires, Venancio Deulofeu was elected chairman; Establier acted as advisory secretary. Four sessions were held in all.

All present agreed that the project to institute an International Andean Year was of great importance, not only because of its extent and because of the scientific results which could be obtained but also because of the number of scientists involved and the expected participation by countries outside South America. It was also felt that a project of this magnitude would have a favorable impact on the progress of science and the future scientific development of most of the South American countries.

Discussions dealt with the fields in which it would be desirable to have activities during the International Andean Year. It was tentatively decided that it would be possible and convenient to work in the following subject areas: geology; botany; geophysics; human biology; zoology; human ecology; geomorphology, including glaciology; high-altitude physics;

soil sciences; geography; agronomic sciences (in collaboration with the U.N.'s Food and Agriculture Organization); sociology and ethnography (both in collaboration with the Social Sciences Institutes); archeology; anthropology; and economics [in collaboration with the Economic Commission for Latin America (CEPAL)].

In each of these fields some subdivisions were outlined, and, as examples of the type of work which would be involved, some specific projects were mentioned. For instance, it was suggested that in studying the geology of the Andes it would be desirable to concentrate on the evolution of the Andean range, especially the tectonic and magmatic cycles of the Andean syncline; on tertiary and quaternary vulcanism; and on magmatic provinces in the Andes.

A larger meeting was planned for December 1961. This will be held in Santiago de Chile, to consider some reports to be presented by the scientists participating in the meeting in Buenos Aires and to elaborate and develop the specific projects in each scientific field.

In the meantime, the UNESCO Scientific Office in Montevideo will start compiling a bibliography on research done on the Andes and collecting the names of scientists who have been active in that field, or who, because of their training, will be able to participate in the activities planned for the International Andean Year.

Further information on this project can be obtained from Dr. A. Establier, Centro de Cooperación Científica de la UNESCO para América Latina, Boulevard Artigas 1320, Montevideo, Uruguay.

V. DEULOFEU

Parera 77, Buenos Aires, Argentina

### Forthcoming Events

#### September

11-15. Radioecology, symp., Fort Collins, Colo. (Miss A. Barker, American Inst. of Biological Sciences, 2000 P St., NW, Washington 6)

11-16. International Union for the Scientific Study of Population, 12th congr., New York, N.Y. (C. V. Kiser, Milbank Memorial Fund, 20 Wall St., New York 5)

11-16. University of Hong Kong, intern. scientific congr., Hong Kong. (University of Hong Kong, Hong Kong)

11-19. International Congr. of Navigation, 20th, Baltimore, Md. (E. W. Adams, Jr., 22 Light St., Baltimore 2)



11-21. International Cloud Physics Conf., Canberra and Sydney, Australia. (E. G. Bowen, Commonwealth Scientific and Industrial Research Organization, University Grounds, Sydney)

12-13. International Federation of Surgical Colleges and Societies, 4th annual Oslo, Norway. (K. Cassels, IFSC Office, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2)

12-15. International Pharmaceutical Federation, 19th general assembly, Athens, Greece. (J. H. M. Winters, Alexanderstraat 11, The Hague, Netherlands)

12-15. Mass Spectrometry, conf., Oxford, England. (W. J. Brown, Instrumentation Div., A.E.I. (Manchester) Ltd., Trafford Park, Manchester 17, England)

13-16. European Congr., of Gerontology, 3rd, Amsterdam, Netherlands. (A. J. S. Douma, Haanplein 8, The Hague, Netherlands)

14-17. Chemotherapy, 2nd intern. symp., Naples, Italy. (P. Preziosi, Casella postale 266, Naples)

14-20. High Energy Physics, intern., Aix-en-Provence, France. (E. W. D. Steel, European Organization for Nuclear Research, Geneva 23, Switzerland)

15-20. World Medical Assoc., 15th general assembly, Rio de Janeiro, Brazil. (L. H. Bauer, 10 Columbus Circle, New York 19)

16-20. German Soc. for the History of Medicine, Physical Science and Technology, Augsburg, Germany. (G. Mann, Secretary, Wilhelmplatz 7, Bonn, Germany)

16-27. International Scientific Film Assoc., 15th congr., Rabat, Morocco. (M. Afifi, 85 Ibn Toumert, Rabat)

18-2. World Meteorological Organization, Commission for Aerology, 3rd session, Rome, Italy. (WMO, 1 Avenue de la Paix, Geneva, Switzerland)

18-20. Applied Spectroscopy, 8th symp., Ottawa, Canada. (R. Lauzon, Div. of Pure Chemistry, National Research Council, Ottawa, Ont.)

18-21. Embryological Conf., 5th intern., London, England. (L. Brent, Dept. of Zoology, University College, London, Grover St., London, W.C.1)

18-22. International Congr. of Neuro-radiology, 6th Rome, Italy. (E. Valentino, CIT, Ufficio Congressi, Piazza Colonna 193, Rome)

18-23. Speleology, 3rd intern. congr., Vienna, Austria. (Generalsekretariat des 3rd Internationalen Kongresses für Speläologie, Obere Donaustr. 99/7/1/3, Vienna 2)

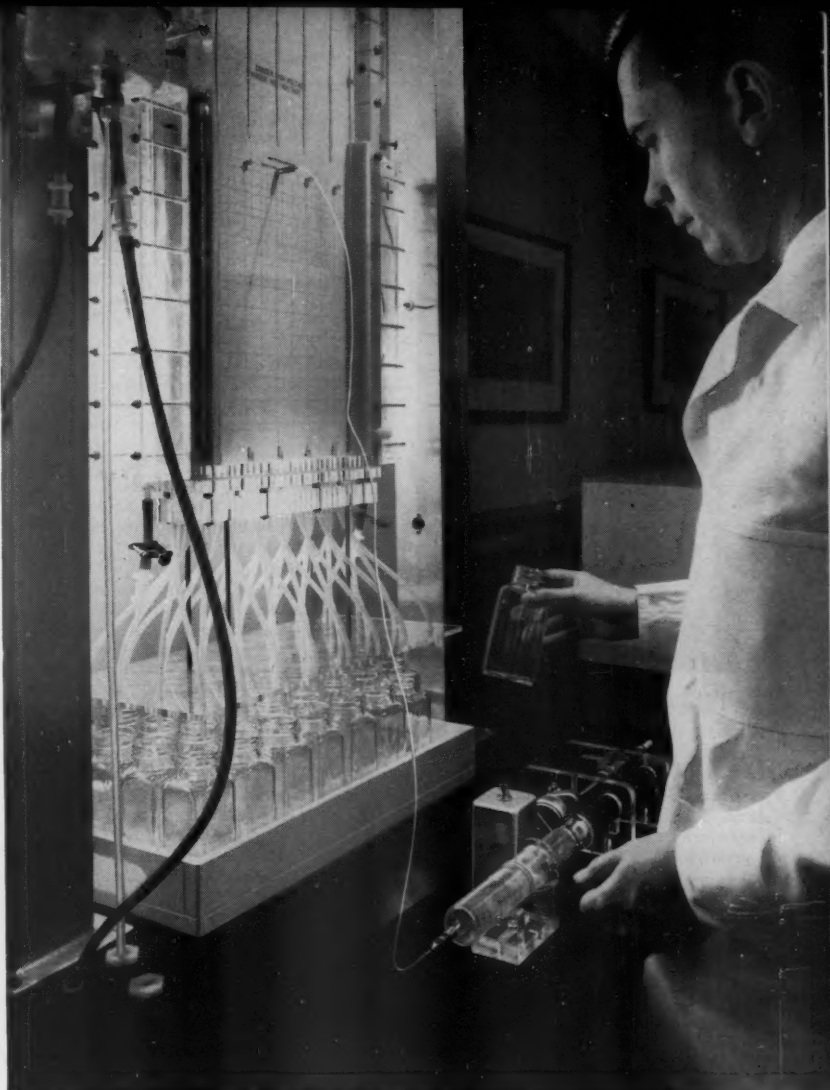
18-25. International Seaweed Symp., 4th, Biarritz, France. (M. Barriety, Centre Scientifique, B. P. 28, Biarritz.)

19-21. International Mechanical Pulp Conf., 4th, Chicago, Ill. (J. H. Perry, Norton Co., Worcester, Mass.)

19-22. Australian Conf. on Food Technology, Homebush (near Sydney), Australia. (T. B. Partridge, Australian Scientific Liaison Office, 1907 K St., NW, Washington 6)

19-22. International Office of Documentation of Military Medicine, 23rd session, Athens, Greece. (Intern. Committee of Military Medicine and Pharmacy, Hôpital Militaire, 79 rue Saint Laurent, Liège, Belgium)

25 AUGUST 1961



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J-173



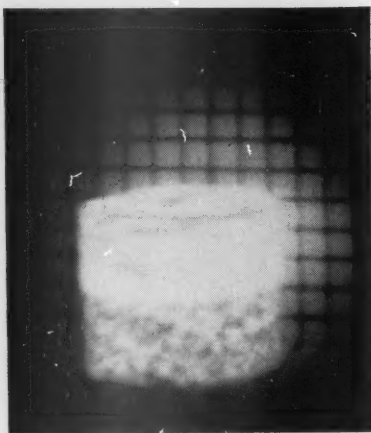
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19-29. International Conf. on Fish Nutrition, Washington, D.C. (FAO, Intern. Agency Liaison Branch, Office of the Director General, Viale delle Terme di Caracalla, Rome, Italy)

20-21. Industrial Electronics, symp., Boston, Mass. (W. M. Trenholme, General Electric Co., West Lynn, Mass.)

21-22. Air Pollution Control Assoc., annual, Louisville, Ky. (R. Bourne, APCA, Room 2, City Hall, Louisville)

21-22. Conference on Radiofrequency Spectroscopy in Solids, Bangor, Wales. (Physical Soc., 1 Lowther Gardens, Prince Consort Rd., London, S.W.7, England)

21-23. French Medical Congr., 33rd, Paris. (C. Laroche, 34 rue de Bassano, Paris 8)

24-27. American Inst. of Chemical Engineers, Lake Placid, N.Y. (E. R. Smoley, 30 School Lane, Scarsdale, N.Y.)

25-29. European Committee of Liaison for Cellulose and Paper, symp., Oxford, England. (British Paper and Board Makers' Assoc., Technical Section, St. Winifred's, Welcomes Rd., Kenley, Surrey, England)

25-30. Magnetism and Crystallography, intern. conf., Kyoto, Japan. (Science Council of Japan, Ueno Park, Tokyo)

26-30. European Congr. of Aviation Medicine, 6th, Paris, France. (CERMA, 5 bis Avenue de la Porte de Sèvres, Paris)

27-3. International Union of Theoretical and Applied Mechanics, Kiev, U.S.S.R. (Y. A. Mitropolsky, Scientific Committee, Kalinin pl. 6, Mathematical Inst., Kiev)

28-29. European Conf. of Chemical Engineers, Toulouse, France. (Soc. of Industrial Chemistry, 28 rue Saint-Dominique, Paris 7, France)

### October

1-3. Council for Intern. Organizations of Medical Sciences, Paris, France. (CIOMS, 6 rue Franklin, Paris 16)

1-4. Process Engineers, annual, Vienna, Austria. (Osterreichischer Intenieur- und Architektenverein, Eschenbachgasse 9, Vienna 1)

1-5. Electrochemical Soc., Detroit, Mich. (Electrochemical Soc., Inc., 1860 Broadway, New York 23)

1-7. International Special Committee on Radio Interference, plenary session, Philadelphia, Pa. (S. D. Hoffman, American Standards Assoc., 10 E. 40 St., New York 16)

1-8. International Congr. of Industrial Chemistry, 33rd, Bordeaux, France. (Société de Chimie Industrielle, 28 rue Saint-Dominique, Paris 7, France)

2-4. Communications Symp., 7th natl., Utica, N.Y. (R. K. Walker, 34 Bolton Rd., New Hartford, N.Y.)

2-7. International Astronautical Federation, 12th congr., Washington, D.C. (American Rocket Soc., 500 Fifth Ave., New York 36)

2-7. Inter-Regional Leprosy Conf., Istanbul, Turkey. (WHO, Regional Office for Europe and Regional Office for the Eastern Mediterranean, 8 Scherfigsvej, Copenhagen Ø, Denmark)

2-7. Climatic Change, symp., Rome, Italy. (UNESCO, Place de Fontenoy, Paris 7, France)

2-11. International Council for the Exploration of the Sea, 49th annual, Copen-

hagen, Denmark. (Charlottenlund Slot, Charlottenlund, Denmark)

3-5. Physics and Nondestructive Testing, symp., Argonne, Ill. (W. J. McGonagle, Argonne Natl. Laboratory, 9700 S. Cass Ave., Argonne)

3-8. Aerosol Congr., 3rd intern., Lucerne, Switzerland. (Federation of European Aerosol Assocs., Waisenhausstrasse 2, Zurich, Switzerland)

4-10. Latin American Congr. of Electroencephalography, 5th, Mexico, D.F. (J. Hernandez Paniche, Instituto Mexicano de Seguro Social, Hospital La Raza, Mexico, D.F.)

4-10. Latin American Congr. of Neurosurgery, 9th, Mexico, D.F. (J. H. Mateos, Tonalá No. 15, Mexico 7, D.F.)

6-7. American Medical Writers' Assoc., New York, N.Y. (S. O. Waife, P.O. Box 1796, Indianapolis 6, Ind.)

6-8. Therapeutics, 7th intern. congr., Geneva, Switzerland. (P. Rentchnick, Case Postale 229, Geneva 2)

8-10. Zooplankton Production, symp., Copenhagen, Denmark. (J. H. Frazer, Marine Laboratory, P.O. Box 101, Victoria Rd., Aberdeen, Scotland)

8-11. Society of American Foresters, Minneapolis, Minn. (H. Clepper, SAF, 425 Mills Bldg., Washington 6)

8-13. American Acad. of Ophthalmology and Otolaryngology, Chicago, Ill. (W. L. Benedict, 15 Second St., SW, Rochester, Minn.)

9-11. National Electronics Conference and Exhibition, 17th annual, Chicago, Ill. (NEC, 228 N. La Salle St., Chicago, 1)

9-12. Instrument Symp. and Research Equipment Exhibit, 11th annual, Bethesda, Md. (J. B. Davis, Natl. Institutes of Health, Bethesda 14)

9-12. Water Pollution Control Federation, 34th annual, Milwaukee, Wis. (R. E. Fuhrman, 4435 Wisconsin Ave., NW, Washington 16)

9-13. American Rocket Soc., space flight meeting, New York, N.Y. (ARS, 500 Fifth Ave., New York 36)

9-13. Luminescence of Inorganic and Organic Systems, intern. conf., New York, N.Y. (Miss G. M. Spruch, New York Univ., Washington Sq., New York 3)

10-12. Nuclear Reactor Chemistry, 2nd conf., and Analytical Chemistry in Nuclear Reactor Technology, 5th conf., Gatlinburg, Tenn. (Oak Ridge Natl. Laboratory, P.O. Box X, Oak Ridge, Tenn.)

10-20. International Committee for Biological Control, Tunis. (P. Grison, Laboratoire de Biocénologie et de Lutte Biologique, La Minière, par Versailles (S.-et.-O.), France)

11-13. Gaseous Electronics Conf., American Physical Soc., Schenectady, N.Y. (C. J. Gallagher, General Electric Research Laboratories, Schenectady, N.Y.)

11-14. Tau Beta Pi Assoc., Cincinnati, Ohio. (R. H. Nagel, Univ. of Tennessee, Knoxville)

11-14. Western Inst. on Epilepsy, 13th annual conf., San Antonio, Tex. (F. Risch, 3097 Manning Ave., Los Angeles, Calif.)

12-13. Congress of Neurological Surgeons, New York, N.Y. (E. Weiford, 4706 Broadway, Kansas City 12, Mo.)

12-29. Pacific Intern. Trade Fair, 2nd, technical meetings, Lima, Peru. (PITF, P.O. Box 4900, Lima)

(See issue of 18 August for comprehensive list)

## New Products

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Neither Science nor the writer assumes responsibility for the accuracy of the information. All inquiries concerning items listed should be addressed to the manufacturer. Include the department number in your inquiry.

**Temperature programmer**, for gas chromatographs, operates by following a curve traced on a transparent plastic sheet with india ink or a strip of black tape. The program sheet is placed on a rotating drum. The slope of the curve determines the rate of rise; a zero potentiometer determines the starting temperature; a span potentiometer determines the heat rise. Rate of increase of temperature may be as high as 30° to 60°C per minute. A single program may include step functions and curvilinear rates of rise interrupted by intervals of isothermal operation while closely spaced peaks are being eluted. (Beckman Instruments Inc., Dept. Sci325, 2500 Fullerton Rd., Fullerton, Calif.)

**Inductance and capacitance meter** is a direct-reading instrument that covers the L and C ranges from 0 to 300  $\mu$ h and 0 to 300 pf, respectively. The total range is covered in five steps; the smallest full-scale range is 0 to 3. Accuracy of  $\pm 3$  percent is said to be maintained with resistance loads of 20 kohm (shunt) and 10 ohms (series) on inductance measurements and 0.1 megohm (shunt) on capacitance measurements. A guard voltage sufficient to drive to 200 pf eliminates effects of stray capacitances. (Solartron Laboratory Instruments Ltd., Dept. Sci319, Cox Lane, Chessington, Surrey, England)

**Frequency meter** is direct reading over the range 3 cy to 1.65 Mc/sec with accuracy said to be  $\pm 0.1$  percent. Input sensitivity is 20 mv, and discriminator residual noise is 100 db below full scale. A d-c output for operating a recorder is provided. (General Radio Co., Dept. Sci305, West Concord, Mass.)

**Photo-recording paper** is designed to be developed by heat. According to the manufacturer, a visible image forms with as little as 1.5-sec development. Development chemicals are incorporated in the silver photographic emulsion. Enough water is contained in the emulsion and paper support to activate the chemicals. The paper is fast enough for exposure in high-speed oscillograph recorders with high-intensity mercury

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lamps. For permanence longer than several months, the prints may be stabilized or fixed by conventional methods. (Eastman Kodak Co., Dept. Sci-304, 343 State St., Rochester 4, N.Y.)

**Perforated-tape reader** (Fig. 1), for automatic programming with eight-level standard perforated tape, reads 80 bits of information at six tests per second and will locate a test program at a rate of 12 in./sec. The tape is advanced one frame at a time on a switch-closure command signal. A verifier panel shows a full frame hole pattern on the front of the unit. A resettable frame counter is provided. (Electronic Engineering Co. Dept. Sci290, 1601 E. Chestnut Ave., Santa Ana, Calif.)

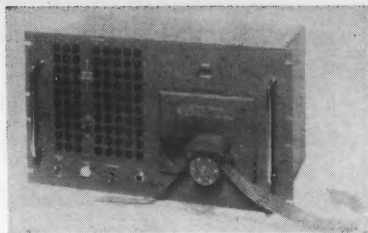


Fig. 1. Perforated-tape reader.

installation, but a minimum grip length is required for proper performance. Electrical specifications include: resistance,  $240 \pm 0.4$  ohms; gage factor,  $2.00 \pm 0.01$ ; maximum excitation, 30 ma and 7 volts, a-c or d-c; output sensitivity,  $0.5 \mu\text{v/volt per } 10^{-6}$  in. Accuracy is said to be within  $\pm 1$  percent of allowable bolt load. (Strainsert Co., Division of Plyphase Instrument Co., Dept. Sci307, E. 4 St., Bridgeport, Pa.)

**Strain-measuring bolt** consists of an electric strain gage bonded and sealed in a small hole along the longitudinal neutral axis of the bolt. It is designed to indicate continuously tensile stress or load induced by tightening or otherwise loading or unloading the bolt. According to the manufacturer, no reduction in allowable bolt load is imposed by either the drilled hole or the gage

**Synchro standard** is electrically equivalent to an accurate ideal synchro transmitter. The standards are connected in the circuit exactly as are synchro transmitters. Output angle is selected by a single detented control

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**Digital voltmeter** features capability of averaging applied voltage over a definite selected sample period. Range, sample period, and sample rate can be programed externally by contact closures. Binary-coded decimal output is provided to drive recording and control equipment.

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AAAS Symposium Volume No. 64

Edited by R. F. Sognaes

July 1960

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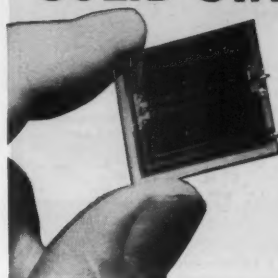
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Applications for the above position, including a curriculum vitae, the titles of publications, a recent photograph and the names of three referees, should be sent to the DEAN OF MEDICINE, UNIVERSITY OF ALBERTA, EDMONTON, ALBERTA, CANADA. 9/1

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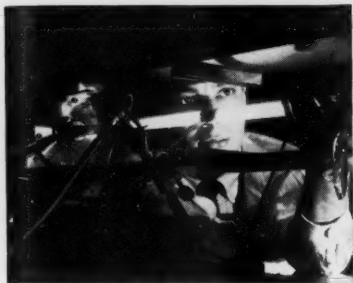
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# What was Bell Telephone Laboratories doing ON FRIDAY, JUNE 30, 1961?



It was exploring the communications possibilities of the gaseous optical maser—a device which generates continuous coherent infrared radiation in a narrow beam.



It was preparing an experiment in world-wide communications using "active" satellites powered by the solar battery, a Bell Laboratories invention.



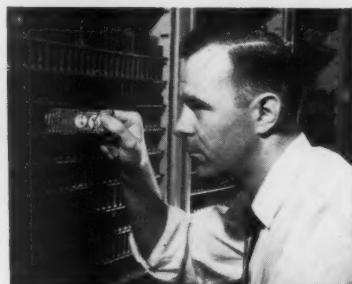
It was completing the development of a new "heavy route" Long Distance microwave system capable of handling over 11,000 two-way conversations at once.



It was developing an anti-missile defense system designed to detect, track, intercept and destroy an enemy ICBM—in a matter of minutes.



It was demonstrating the potentialities of the superconducting compound of niobium and tin for generating, with little power, magnetic fields of great strength.



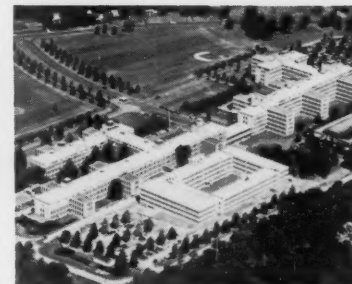
It was experimenting with an electronic central office at Morris, Ill., which is capable of providing a wide range of new telephone services.



It was perfecting the card dialer which permits, through insertion of a punched card into a slot, automatic dialing of frequently used numbers.



It was developing improved repeaters or "amplifiers" to increase greatly the capacity and economy of undersea telephone cable systems.



It was continuing its endless search for new knowledge under the leadership of scientists and engineers with world-wide reputations in their chosen fields.

Bell Laboratories scientists and engineers work with every art and science that can benefit communications. Their inquiries range from the ocean floor to outer space, from atomic physics to the design of new telephone sets, from the tiny transistor to massive transcontinental radio systems. The goal is constant—ever-improving Bell System communications services.

## BELL TELEPHONE LABORATORIES

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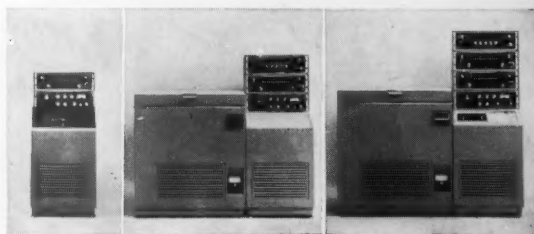
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**Model 701**

**Model 702**

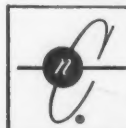
**Model 703**

*Model 701—manual operation, shown with 8250 scaler*

*Model 702—manual, temperature-controlled operation, shown with 8250 scaler and 8600 timer*

*Model 703—automatic, temperature-controlled operation, shown with two 8250 scalars, 8600 timer and 8401 digital recorder*

**Please request literature on these integrated systems.**



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